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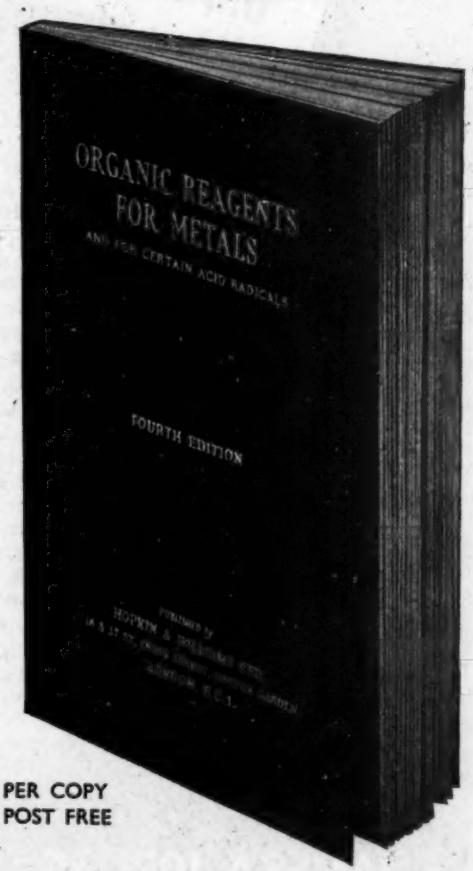


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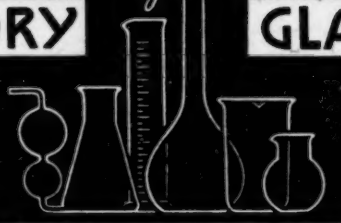

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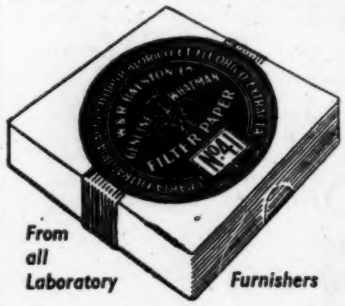


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JOURNAL
OF
THE CHEMICAL SOCIETY.

# 1. *A Method for the Continuous Measurement of the Local Concentration of Atmospheric Ozone.*

By E. GLUCKAUF, H. G. HEAL, G. R. MARTIN, and F. A. PANETH.

A semiportable apparatus has been devised for the continuous recording, over periods up to 24 hours, of the local concentration of atmospheric ozone.

The principle of the method is the liberation of iodine from buffered potassium iodide solution, and its electrometric titration at short intervals with very dilute sodium thiosulphate solution. The small current resulting from the depolarisation of a pair of platinum electrodes by the iodine is amplified by a two-stage valve amplifier, and made to actuate the automatic burette, containing the thiosulphate solution, when the iodine concentration reaches a given value.

EDGAR and PANETH (*Nature*, 1938, **142**, 112; J., 1941, 511, 519) described a method for concentrating atmospheric ozone to such an extent as to make its chemical determination possible. The main merit of the process lay in the proof it afforded, by chemical and spectroscopic means, that the oxidising agent of the atmosphere which was measured by its action on potassium iodide actually was ozone; the process was, however, cumbersome and too slow to allow for more than one or two determinations of atmospheric ozone per day.

In the course of routine measurements it is unnecessary to identify the ozone each time by specific tests; it will suffice to check the correctness of the method by comparison with a standard procedure whenever this seems necessary. Having once established such a standard method for the measurement of the local concentration of atmospheric ozone, we set out to develop a simpler one which would enable us to follow up the variations in the ozone content of air as quickly as meteorological interests demand, *i.e.*, every few minutes. Our method is based on the reaction with potassium iodide of the ozone present in the atmosphere, without previous concentration, the iodine liberated being detected by its depolarising effect on a platinum cathode. Since publishing a preliminary note on this electrochemical method for the rapid determination of atmospheric ozone (Gluckauf and Paneth, *Nature*, 1941, **147**, 614) we have succeeded in making the recording of the results automatic. The following is a description of the method at present in use at Durham for this purpose. As, for meteorological reasons, it will be desirable to carry out such recordings at various places, we paid special attention to the necessity of constructing a portable apparatus which can easily be set up, even under primitive conditions. With the apparatus described here, measurements of the local concentration of ozone outside the Durham Science Laboratories have been made at intervals over a period of several months. These experiments have had to be discontinued for the time being.

The meteorological significance of the results obtained so far will be discussed by one of us (E. G.) in the Quarterly Journal of the Royal Meteorological Society.

## EXPERIMENTAL.

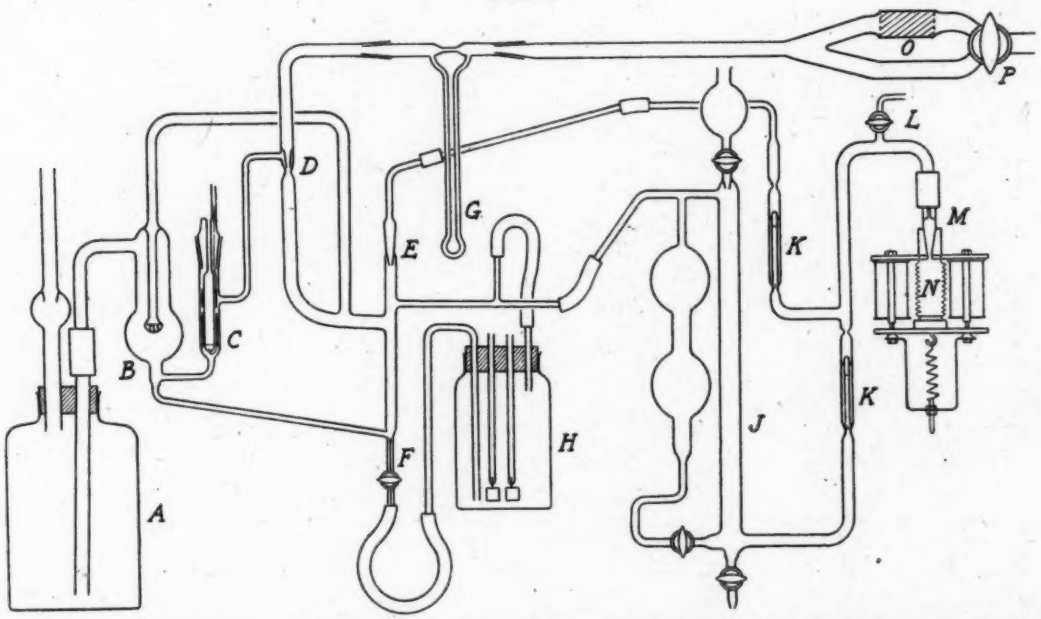
*Method.*—The main features of our method are the absorption of the ozone in sprayed buffered potassium iodide solution, and electrometric titration of the liberated iodine with sodium thiosulphate solution. By means of an electrical relay system, the apparatus is made to function automatically, and to give a continuous record of the ozone concentration and its changes over a period of up to 24 hours.

Apart from ozone, the only substances in the atmosphere likely to liberate iodine from potassium iodide are hydrogen peroxide and nitrogen peroxide. There is little evidence for the existence of the former in air, and, in any case, its action upon potassium iodide solution is so slow that it would only become appreciable during a very long run. As regards nitrogen peroxide we have made several concordant experiments in which a known quantity of the pure gas was allowed to flow slowly into the air-stream from a capillary. With the buffered potassium iodide solution used, the quantity of iodine liberated by nitrogen peroxide is not more than 2% of that calculated from the equation $NO_2 + 2H^+ + 2I^- = H_2O + NO + I_2$. This is not surprising, as the hydrogen ions required for this reaction are kept by the buffer at the low concentration of $10^{-7}$. If the concentration of nitrogen peroxide is high (approx. $10^{-5}$ c.c. per c.c. of air), iodine is liberated with much greater efficiency, probably on account of local acidification by the reaction $2NO_2 + H_2O = 2H^+ + NO_3^- + NO_2^-$, which becomes relatively more frequent at higher concentrations of nitrogen peroxide. Since the concentration of this gas in the atmosphere is of the same order as that of ozone ($10^{-8}$; see J., 1941, 519), its effect may safely be neglected.

*Apparatus* (Fig. 1).—Air from outside the building (on the west side of the Durham Science Laboratories) is drawn by an electric suction pump into the apparatus at a rate of 30 l./min. All tubes carrying the air before its mixing with the solution are of glass, and where movable connections are necessary these are made with ground joints. Grease on the joints, and rubber connections are avoided because of their destructive effect upon the ozone. The air-stream passes from *P* to *A* through a specially designed absorption system, where it atomises the potassium iodide solution into a

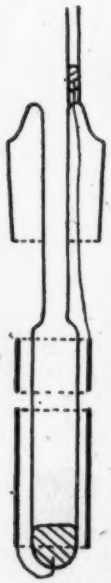
fine spray at the jet *D*, and produces a rapid circulation of the solution past the electrodes *C*. This arrangement gives extremely thorough mixing, but involves the gradual loss of water by evaporation and of potassium iodide solution as spray. The diminution of the bulk of solution caused by evaporation is compensated by connecting the absorption vessel to a reservoir, *H*, of potassium iodide solution, which siphons over and, entering the absorption vessel through a

FIG. 1.




capillary *F*, maintains a nearly constant level. The spray is trapped and returned to the main stream of liquid by the spray trap *B*, in which the air passes through a small glass basket loosely packed with glass-wool. This trap must not be so low that it always contains a large bulk of solution, for this would give rise to irregularities of mixing with the main stream; nor must it be so high that bubbles of air pass into the liquid stream from it. The correct height can only be found by trial, but the figure is approximately to scale, and may serve as a guide, if the rate of air-flow is similar to that in our apparatus.

FIG. 2.

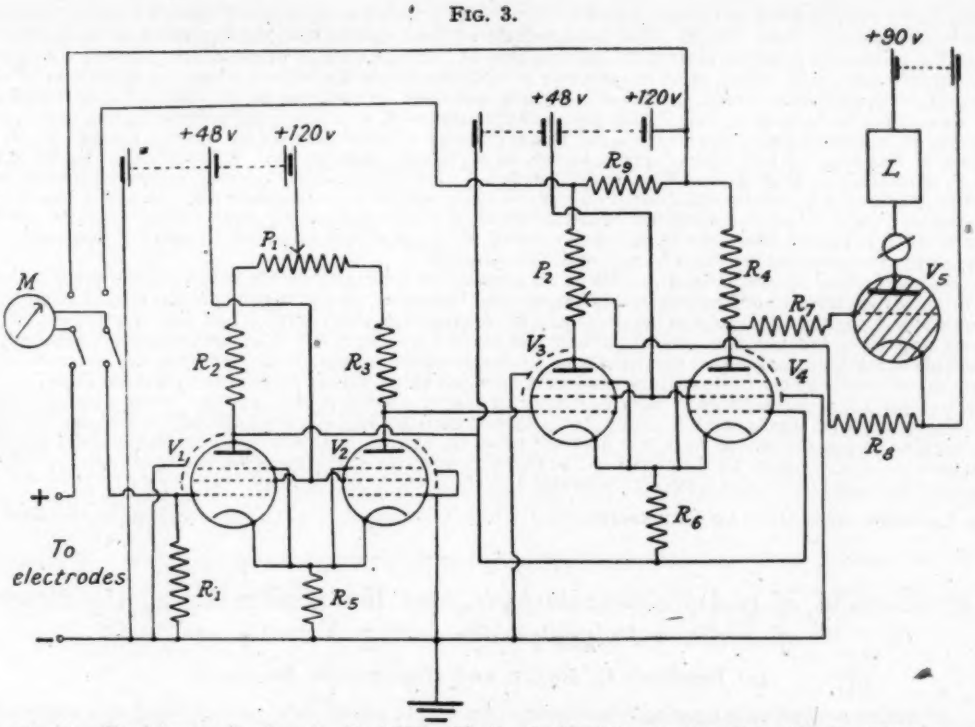


The composition of the potassium iodide solution is as follows: potassium iodide, 100 g.; sodium phosphate, $NaH_2PO_4.H_2O$, 1·38 g.; sodium hydroxide, 0·20 g.; water, 500 c.c. The liberated iodine is determined electrochemically by its depolarising action on a pair of polarised platinum electrodes (Foulk and Bawden, *J. Amer. Chem. Soc.*, 1926, **48**, 2045). The current which it causes to flow is amplified, and works a relay, which results in the addition of a small fixed volume (about 0·3 c.c.) of N/2000-sodium thiosulphate solution, from the automatic burette *J*, through the jet *E*.

Considerable difficulty was experienced in designing a suitable amplifier. The well-known instability of simple D.C. amplifiers led us to try supplying the electrodes with low-voltage A.C., but the polarised system then behaved as a high-capacity electrolytic condenser, and passed a large current in the absence of free iodine. It was therefore necessary to devise some satisfactory method of amplifying the small direct current (~6 microamp., convertible by means of a resistance to a maximum potential difference of ~6 mv.) obtained from the depolarised electrodes. Two high-magnification stages are needed to bring this up to a value sufficient for operation of the relay. Battery fluctuations had to be compensated for by the use of a balanced bridge circuit in each stage. Finally, the problem of biasing the bridge valves automatically, which would be impossible by using a separate bias resistance for each valve, since this arrangement would cause the partial cancellation of the applied E.M.F., was simply solved by using a common bias resistance for each pair of valves. In this way the influence of the bias resistance in compensating for the applied E.M.F. was balanced out by applying it to both bridge valves at once, and correct biasing was achieved, with additional stability and no loss in sensitivity.

*Electrodes* (Fig. 2).—The most suitable form for these has been ascertained by trial. They are maintained at such a small potential difference (0·1 v.) that they are ordinarily completely polarised, and no current flows. In the presence of free iodine, the hydrogen layer on the cathode is oxidised, causing depolarisation. A current passes, of such a value that the rate of production of hydrogen on the cathode surface is exactly equal to its rate of removal by the iodine. In order to obtain the maximum current for a given amount of iodine in the solution, and so to minimise the amplification required, it is clearly necessary to bring as much of the iodine as possible into contact with the cathode surface in a given time. This object is achievable by observing the following requirements: (1) The total bulk of the solution must be kept low, and the iodine concentration correspondingly high (approx. $10^{-6}$ N). (2) The cathode surface must be as large as practicable. (3) A rapid flow of solution must be maintained past the cathode. In practice, (1) and (2) can only be satisfied by a compromise; moreover, we found that large electrodes gave trouble because they prevented rapid mixing of the thiosulphate after each addition, and also because they permitted the passage of a large steady current in the absence of free iodine. The electrode system illustrated was as sensitive as any examined, responded almost instantaneously to the thiosulphate additions, and gave zero current in the absence of free iodine. The electrodes are cylinders of platinum foil. They fit loosely round the glass tube which carries them, so as to allow the solution access to both surfaces. They are supported only by the connection wires. Both electrodes were of 37 mm. circumference, and the anode (upper electrode) and cathode were respectively 9 and 24 mm. high. Connections to the electrodes are made by means of mercury, in the central tube for the cathode, and the side tube for the anode.

FIG. 3.




*Key to Fig.* 3. (Resistances in ohms.) $R_1$, 1000; $R_2$, $R_3$, $R_4$, 30,000; $R_5$, $R_6$, 200; $R_7$, $R_8$, 100,000; $P_1$, 5,000; $P_2$, 30,000; $R_9$, shunt for meter; $V_1$, $V_2$, $V_3$, $V_4$, Cossor MS 4 PEN; $V_5$, Osram GT1B; *M*, microammeter reading 0—50 microamps.; *L*, magnetic relay.

It is advisable to clean the surface of the electrodes before use, by heating them to whiteness in a hydrogen flame.

The suction pump used in our apparatus is an Edwards "Type 4, Compressor and Vacuum Pump." In order to prevent fouling of the mechanism with potassium iodide spray from the absorption apparatus, the air is bubbled through a small depth of water in wash-bottle *A* before entering the pump.

*Automatic Burette* (Fig. 1, *JKLMN*).—This is constructed of Pyrex glass, except the bellows *N*, which are of copper, and the short metal capillary tube *M*, serving to prevent too violent ejection of the thiosulphate solution, which would result in the rubber joints being loosened. The connection between *M* and the glass portion of the burette is made with pressure-tubing. Direct connection with vacuum wax is satisfactory if the magnets are run from direct current, but the wax is soon cracked by the vibration set up when alternating current is used. In a semiportable apparatus it is a great convenience to use mains A.C. wherever possible, and we have therefore used a rubber joint in our apparatus. The valves *K* are ordinary ground-in glass valves weighted with mercury. These need to be of a somewhat better fit than the usual mercury float-valves, but if they are symmetrical and carefully ground, the leakage through them is negligible. The tap *L* facilitates filling of the burette.

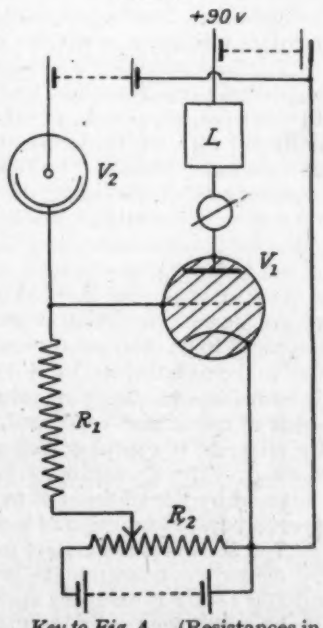
The N/2000-sodium thiosulphate solution is obtained by two dilutions of N/10-solution. It is not very stable, and must be made up afresh for every run. It can be standardised by titration in a separate vessel against the iodine liberated by very dilute potassium dichromate solution. The end-point is best determined electrometrically, the liquid being stirred by an air-stream.

A simpler method is to pass a known electric current through the potassium iodide solution in the apparatus, by means of two small separate platinum electrodes, while destroying the ozone of the air on a charcoal filter. The iodine liberated at the anode is then titrated continuously and automatically; at the iodine concentrations attained, no measurable reduction of it takes place at the cathode. In this manner the calibration values are obtained on the same record, at the expense of a few minutes of ozone measurement.

To allow for the small quantity of iodine entering the vessel continuously with the fresh potassium iodide solution, it is useful to make a blank run, by destroying the ozone with a filter containing about 5 oz. of active charcoal (Fig. 1, *O*). The large tap *P* (Fig. 1) allows air to be drawn into the apparatus either directly or through the filter.

*Amplifier, Relay System, and Recording Apparatus.*—The electrode voltage, 0·1 v., is provided by a single dry cell with a potential divider. The current is amplified by means of a two-stage direct-current amplifier, stabilised by using a bridge circuit in each stage (Fig. 3). The voltage available for amplification is up to 10 mv. (10 microamps. electrode current, with a resistance of 1000 ohms in the circuit). The amplification is approximately 3,000, and the voltage output up to 30 v. This is used to trigger a gas-filled relay valve, the anode current from which operates a delayed-action magnetic relay, causing

FIG. 4.




*Key to Fig.* 4. (Resistances in ohms.) $R_1$, 250,000; $R_2$, 200,000; $V_1$, Osram GT1B; $V_2$, Osram CMG8; *L*, magnetic relay.

an injection to be made by the automatic burette. Every such injection is recorded upon a rotating drum, operated by a geared-down electric clock motor. The total volume of thiosulphate used during a run is found by reading the burette, and the volume per injection is given by dividing this by the total number of injections. Hence the average ozone concentration over any given period, short or long, can be calculated from the intervals between injections on the record.

The amplifier requires some time to attain equilibrium, and must be switched on at least 1½ hours before use. It is necessary to earth it as indicated, and if this precaution is observed it is electrically and mechanically very stable. Potentiometer $P_1$ is set to balance the first bridge; this is done by adjustment until the current through $V_3$, as measured by the meter $M$, is about 1·5 milliamps., approximately equal to that through $V_4$. This adjustment need not be made exactly. $P_2$ is then set so that the gas-filled relay "strikes" when the electrode current, measured by the same meter on a different switch setting, reaches the desired value; 6—7 microamps. is a suitable value, but, again, exact adjustment is not necessary. Once made, the amplifier adjustments need not be altered for days. The magnetic relay remains on for 5 secs. when actuated, then breaks the anode circuit of the gas-filled valve. This delay is necessary in order to allow time for the thiosulphate injection to mix with the solution.

*Galvanometer–Photocell System* (Fig. 4).—This is an alternative arrangement for operating the relay system, which was used in an earlier form of our apparatus, before we had succeeded in amplifying the electrode current sufficiently to work a relay. It has the advantage of being simpler in construction, and operates well when carefully set up, but it is less compact and more troublesome to adjust than the valve amplifier; nor is it conveniently transportable. The simple principle of its operation is that the light-spot from a sensitive mirror galvanometer in the electrode circuit falls upon the photocell when the electrode current reaches the desired value, and so triggers the gas-filled relay.

*Electric Current Supplies.*—The only external source of supply needed is A.C. mains. From this are supplied the burette magnets, recorder motor, and recorder stylus direct, and the valve heaters through a transformer giving 4 v. The four amplifier valves are heated from one filament winding, the centre of which is earthed, and the gas-filled relay from a separate winding, with its centre connected to the negative side of the relay high-tension battery. This is done to avoid a large potential difference between the heater and the cathode of the relay.

SCIENCE LABORATORIES, DURHAM UNIVERSITY. [*Received, September 23rd*, 1943.]

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## 2. *Preparation of* p-*Aminobenzaldehyde, and the Mechanism of the Reactions of Sodium Polysulphides with* p-*Nitrotoluene.*

By HERBERT G. BEARD and HERBERT H. HODGSON.

An improved method of preparing *p*-aminobenzaldehyde in about 75% yield is based on a study of the reactions of *p*-nitrotoluene with sodium sulphide and polysulphides.

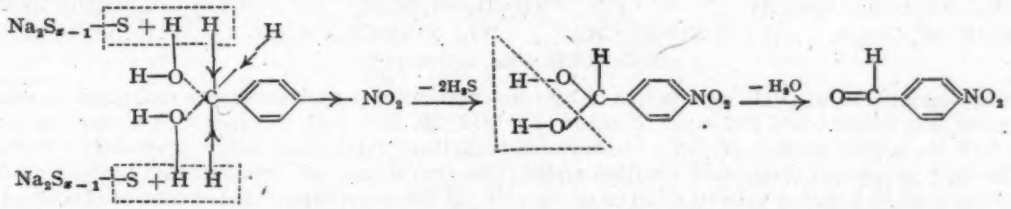
WHEN *p*-nitrotoluene reacts with a solution of sulphur in aqueous alcoholic sodium hydroxide (Geigy, D.R.-P. 86,874; Friedländer and Lenk, *Ber.*, 1912, **45**, 2083), *p*-aminobenzaldehyde and *p*-toluidine are formed. A study of the mechanism of this reaction has shown that the average yield of each product from 100 g. of *p*-nitrotoluene is 40 g. and that two simultaneous reactions are proceeding with approximately equal velocities, namely, (*a*) an oxidation-reduction, which produces *p*-aminobenzaldehyde, and (*b*) straight reduction to *p*-toluidine. The balance of the *p*-nitrotoluene (*ca.* 4%) is recovered unchanged, and no evidence of the intermediate formation of stilbene derivatives has been obtained.

In the preparation according to Geigy, sodium hydroxide (100 parts) and sulphur (60 parts) were dissolved in boiling aqueous alcohol, and it was first ascertained experimentally that these quantities did react according to the equation usually given, $6NaOH + 4S = 2Na_2S + Na_2S_2O_3 + 3H_2O$. Since sodium thiosulphate does not react with *p*-nitrotoluene, it was concluded that sodium sulphide or a polysulphide used initially would not only be more efficient than Geigy's mixture, but would more readily provide data for the study of the reaction mechanism. Accordingly, a series of experiments was made in which sodium polysulphides, $Na_2S_x$ ($x = 1$ to 5), reacted under identical conditions with *p*-nitrotoluene in aqueous alcoholic sodium hydroxide. The yields of *p*-aminobenzaldehyde varied from *ca.* 40% with $Na_2S$ to *ca.* 75% with $Na_2S_4$, and when the sulphur content was raised to $Na_2S_5$, by-products originated in further reactions of the primary amines formed. Of methyl, ethyl, and *n*-propyl alcohol, ethyl alcohol was the most efficient for the oxidation-reduction reaction (*a*); in the absence of an alcohol the yield of *p*-aminobenzaldehyde was only 31%. Free alkali (sodium hydroxide), however, appeared to be even more necessary than alcohol for reaction (*a*), since in its absence (or at small concentrations due to the equilibrium, $Na_2S + H_2O \rightleftharpoons NaOH + NaSH$) the yield of *p*-aminobenzaldehyde was less than 10%. Intermediate polysulphide formation during the reaction with sodium monosulphide was indicated by development of colour and confirmed, after completion of the reaction and removal of organic material by solvents, by analysis, the sulphur being allocated to $Na_2S_2O_3$, NaSH or $Na_2S$, $Na_2SO_4$ (trace only), and polysulphide sulphur. The formation of polysulphide indicated its necessity for reaction (*a*), supporting evidence being obtained by the addition of pyrogallol to the various polysulphide mixtures, whereby removal of polysulphide prevented the formation of *p*-aminobenzaldehyde, the sole product being *p*-toluidine.

The above results clearly indicate that the oxidation of the methyl to the aldehyde group is brought about by the sodium polysulphide, probably on the lines developed by Robinson (J., 1941, 230), the loosely combined sulphur acting as oxidising agent as in the scheme on p. 5.

The hydrogen sulphide produced will be converted into sodium hydrosulphide by the alkali present and, together with the sodium sulphide also present, will then reduce the nitro- to the amino-group. When sodium sulphide is used alone, the sulphur necessary for polysulphide formation will be produced by its reaction with the nitro-group, and subsequent oxidation of the methyl group can then occur. When the amount of sodium sulphide is decreased to the minimum, as when the higher polysulphides are used, the amount of *p*-toluidine

formed becomes the minimum also. Too great an excess of sulphur, however, promotes thionation of the amines first formed (cf. Hodgson and France, J., 1933, 296).



An improved preparation (with R. R. Davies) of *p*-aminobenzaldehyde, by a modification of Geigy's directions, is described, together with one of *o*-chloro-*p*-aminobenzaldehyde from *o*-chloro-*p*-nitrotoluene.

## Experimental.

p-*Aminobenzaldehyde.*—A mixture of *p*-nitrotoluene (10 g.), hydrated sodium sulphide (6·0 g.), sulphur (2·5 g.; ratio of 1 g.-mol. of *p*-nitrotoluene to 0·33 g.-mol. of sodium polysulphide), ethyl alcohol (60 c.c.), sodium hydroxide (4·5 g.), and water (120 c.c.), was refluxed for 90 minutes. The alcohol and *p*-toluidine (1·7 g.) were then removed by steam, and the non-volatile *p*-aminobenzaldehyde (6·6 g.; 74·6%, estimated as *p*-nitrophenylhydrazone) collected and preserved for subsequent use by conversion into the sulphate (cf. Geigy, *loc. cit.*). Alternatively, the steam distillation may be replaced by an ether extraction, and the procedure modified accordingly.

*Yields of* p-*aminobenzaldehyde from* p-*nitrotoluene* (10 g.), *with variations of sodium polysulphide only.*

| Hydrated sodium sulphide, g. | Sulphur added, g. | Formula. | *p*-Aminobenzaldehyde, estimated as *p*-nitrophenylhydrazone. | |
|---|---|---|---|---|
| 6 | 0·0 | $Na_2S$ | 3·0—3·5 g. | 35—40% |
| 6 | 0·8 | $Na_2S_2$ | 4·0 | 45·3 |
| 6 | 1·6 | $Na_2S_3$ | 4·75 | 53·4 |
| 6 | 2·4 | $Na_2S_4$ | 6·35 | 72·0 |
| 6 | 3·2 | $Na_2S_5$ | Contaminated by by-products | |

*Effect of variations of alcohol only in optimum preparation above.*

| Alcohol. | Yield of *p*-aminobenzaldehyde, g. | % |
|---|---|---|
| Methyl | 4·7 | 53·4 |
| Ethyl | 6·6 | 74·6 |
| *n*-Propyl | 5·28 | 59·2 |
| None | 2·74 | 31·8 |

*Preparation of* p-*Amino- and* o-*Chloro*-p-*amino-benzaldehyde by a Modification of Geigy's Process* (with R. R. Davies).—Boiling solutions of *p*-nitrotoluene (68·5 g.; 0·5 g.-mol.) and of *o*-chloro-*p*-nitrotoluene (86 g.; 0·5 g.-mol.) were each treated dropwise during 1 hour with a boiling solution of sulphur (41 g.) in 17% aqueous sodium hydroxide (500 g.); the mixtures were then boiled for a further 2 hours and cooled to 20°. The aldehydes were collected, washed with water (300 c.c.), and recrystallised from 50% acetic acid. The yields of pure products (by nitrite and hydroxylamine estimations) were: *p*-aminobenzaldehyde, 32 g. (52%); *o*-chloro-*p*-aminobenzaldehyde, 35·8 g. (46%).

Technical College, Huddersfield.

[*Received, July 7th*, 1943.]

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## 3. *Analogues of Pantothenic Acid. Part III.* Preparation of Growth-inhibiting Analogues related to* N-*Pantoyltaurine.*

By Jean Barnett.

The preparation of further sulphur-containing substances closely related to *N*-pantoyltaurine, *viz.*, *N*-pantoyl-β-aminoethylthiol, bis(pantoyl-β-aminoethyl) monosulphide, *disulphide*, sulphoxide, and -sulphone, is described. Pantoyltaurine, the sulphonic acid corresponding to pantothenic acid (I), has previously been shown to have antibacterial activity *in vitro* and *in vivo*. None of the analogues now described, when tested *in vitro* against *Lactobacillus arabinosus*, was more active than pantoyltaurine, but the disulphide and the thiol had an almost equal inhibitory action, which was reversed by pantothenic acid. *In vivo* tests against animals infected with *Streptococcus hæmolyticus* gave no indication of activity superior to that of pantoyltaurine.

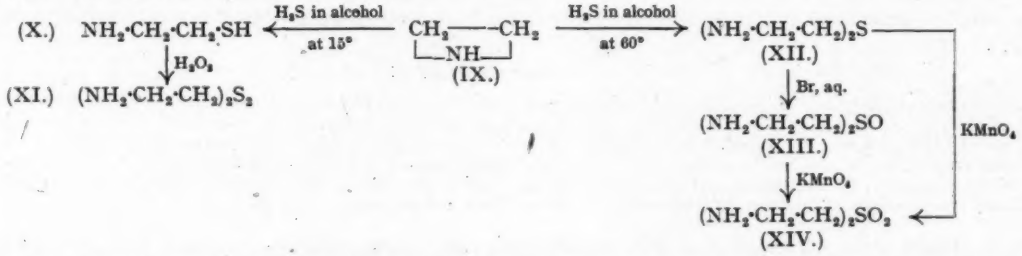
*In vivo* experiments with *N*-pantoyltaurine (McIlwain and Hawking, *Lancet*, 1943, **1**, 449), have shown that only in high doses does it afford protection to animals infected with *Strep. hæmolyticus*. Analogues of pantoyltaurine (II) have therefore been prepared by replacing the sulpho-group with other sulphur-containing groups, in the hope that these substances might produce a greater bacteriostatic effect. The preparation of *N*-pantoyl-β-aminoethylthiol (III), *bis*-(N-*pantoyl*-β-*aminoethyl*) *disulphide* (IV), bis-(*N*-pantoyl-β-aminoethyl) mono-

* Parts I and II, *Biochem. J.*, 1942, **36**, 357, 364.

sulphide (V), bis-(*N*-pantoyl-β-aminoethyl) sulphoxide (VI), and bis-(*N*-pantoyl-β-aminoethyl)sulphone (VII) is now described.

(I.) P·NH·$CH_2$·$CH_2$·$CO_2H$ (II.) P·NH·$CH_2$·$CH_2$·$SO_3H$ (III.) P·NH·$CH_2$·$CH_2$·SH
(IV.) $(P·NH·CH_2·CH_2)_2S_2$ (V.) $(P·NH·CH_2·CH_2)_2S$ (VI.) $(P·NH·CH_2·CH_2)_2SO$ (VII.) $(P·NH·CH_2·CH_2)_2SO_2$
P = OH·$CH_2$·$CMe_2$·CH(OH)·CO·.

The analogues (IV) to (VII) were prepared by condensation of pantolactone (for references to methods of preparation, see Barnett and Robinson, *Biochem. J.*, 1942, **36**, 259) with the appropriate diamino-compound (XI to XIV )in boiling methyl alcohol. Pantoylaminoethylthiol (III) could not be prepared by this method, since the thiol group was completely oxidised under these conditions, and was obtained by heating the components together in a sealed tube in absence of air. In all the experiments, the extent of condensation was measured by a Van Slyke amino-nitrogen estimation.




The method by which the bases required (X to XIV) had been prepared previously from the corresponding phthalimido-compounds (Gabriel, *Ber.*, 1889, **22**, 1137, 3098; 1891, **24**, 1111) was found tedious and difficult. A better method for the preparation of β-aminoethylthiol (X) and bis-β-aminoethyl sulphide (XII) from hydrogen sulphide and ethyleneimine (IX) (Wenker, *J. Amer. Chem. Soc.*, 1935, **57**, 2328), described by Mills and Bogert (*J. Amer. Chem. Soc.*, 1940, **62**, 1173; 1941, **63**, 2363), has been used in the present work. Bis-β-aminoethyl disulphide (XI) was obtained quantitatively from (X) by oxidation with hydrogen peroxide (cf. Gabriel and Leupold, *Ber.*, 1898, **31**, 2837; Mills and Bogert, *loc. cit.*, p. 2363). Bis-β-aminoethyl sulphoxide (XIII) was obtained in quantitative yield by oxidation of bis-β-aminoethyl sulphide with bromine water, and the corresponding sulphone (XIV) in 50% yield by oxidising the sulphide with two equivalents or the sulphoxide with one equivalent of permanganate (cf. Gabriel, *Ber.*, 1891, **24**, 3098).

Bis-(*N*-pantoyl-β-aminoethyl)sulphoxide (VI), obtained from bis-β-aminoethyl sulphoxide by refluxing the components in methyl alcohol for 1 hour, was a yellowish viscous oil. After 3 months, it crystallised and from the semi-crystalline mass, bis-(*N*-pantoyl-β-aminoethyl) disulphide, m. p. 143—144°, was isolated, identical with the material prepared from bis-β-aminoethyl disulphide and pantolactone. This fission of a sulphoxide finds a parallel in the fission of phenylsulphoxyacetic acid to thiophenol and glyoxylic acid (Pummerer, *Ber.*, 1909, **42**, 2282; 1910, **43**, 1401):

$$C_6H_5·SO·CH_2·CO_2H \longrightarrow C_6H_5·SH + CHO·CO_2H$$

If a fission such as that described above took place, the thiol so formed might be spontaneously oxidised to the disulphide. It is, however, clear from the titration of bis-β-aminoethyl sulphoxide with permanganate that no such fission had already taken place when this compound was condensed with pantolactone, otherwise more than one atom of oxygen would have been absorbed, which did not occur. Unfortunately, no initial titration with permanganate had been carried out on the product which, after 3 months' standing, yielded the disulphide. It is therefore not possible to decide whether the fission occurred during the condensation, or on standing for a long period. It is hoped to investigate this reaction further.

Biological tests on these analogues were carried out by Dr. J. Ungar. *In vitro* tests on *Lactobacillus arabinosus* showed that, though none of them was more active than pantoyltaurine, pantoylaminoethylthiol and bis(pantoylaminoethyl) disulphide were highly active as growth inhibitors, having practically the same antagonising effect as pantoyltaurine. The corresponding sulphoxide, monosulphide and sulphone had an inhibiting effect to a less degree; the effect was always reversed by addition of pantothenic acid. It may perhaps be significant that the two most highly active compounds of this series were those in which the ratio of sulphur to nitrogen is approximately the same as for pantoyltaurine, whereas compounds having only half this sulphur content were less active.

*In vivo* tests on rats infected with *Streptococcus hæmolyticus* gave no evidence that these analogues have an activity superior to that of pantoyltaurine; indeed, the results suggested that rats were more susceptible to the influence of the bacteria in the presence of these substances than in their absence. The pantoyl-thiol analogue was highly toxic; the others were well tolerated.

The biological results will be reported in detail elsewhere.

## Experimental.

*β-Aminoethylthiol* (X).—(The successful preparation of this substance from ethyleneimine depends very much on conditions; unless the optimum conditions described below are rigidly adhered to, none is obtained.) An alcoholic

solution of ethyleneimine (dried finally over sodium and redistilled over potassium hydroxide) was run during ½ hour into absolute ethyl alcohol saturated with hydrogen sulphide, kept between 10° and 20°, and shaken continuously while hydrogen sulphide was passing through the liquid. The mixture was left overnight at 10°, and the solvent evaporated in a vacuum. β-Aminoethylthiol was obtained as a hygroscopic white solid, which was sublimed at 70—80°/15 mm. just before use. The purity, as determined by titration with 0·1N-iodine (·SH ⟶ ·S·S·), was 97%.

*Dinitrobenzoyl thioether.* Resublimed β-aminoethylthiol (150 mg.) was dissolved in absolute alcohol (4 ml.), N-potassium hydroxide (1·8 ml.) added, and the mixture added to 1-chloro-2 : 4-dinitrobenzene (400 mg.) in absolute alcohol (2 ml.); an immediate precipitate formed. The solution was refluxed for 3 minutes and filtered hot. On cooling, orange needles (75 mg.) were deposited, m. p. 93·5—94·5° after recrystallisation from absolute alcohol (Found: S, 13·1. $C_8H_9O_4N_3S$ requires S, 13·2%).

N-*Pantoyl-β-aminoethylthiol* (III).—Pure resublimed β-aminoethylthiol (480 mg.) and redistilled pantolactone (820 mg.) were heated in a vacuum in a sealed tube at 100° for 1 hour. The resulting yellow oil was heated at 70° in a vacuum to remove any unchanged thiol. Titration with iodine indicated that the substance was 86% pure, and a Van Slyke estimation showed the presence of 1·7% of free amino-nitrogen, corresponding to 78% condensation.

*Bis-β-aminoethyl Disulphide* (XI).—This was prepared by oxidation of the pure resublimed thiol (10 g.) with hydrogen peroxide (Mills and Bogert, *loc. cit.*). The crude dihydrochloride (yield, 80%), recrystallised from 95% alcohol, gave bis-β-aminoethyl disulphide dihydrochloride in needles, m. p. 200—203°. Gabriel and Leupold (*loc. cit.*) record m. p. 203°, and Mills and Bogert (*loc. cit.*) m. p. 217°. The base was obtained by addition of exactly 1 equiv. of 10% aqueous sodium hydroxide to an aqueous solution of the dihydrochloride and evaporation to dryness in a vacuum at 50°, followed by repeated extraction with hot absolute alcohol.

*Bis-*(N-*pantoyl-β-aminoethyl*) *Disulphide* (IV).—Bis-β-aminoethyl disulphide (6·5 g.) was dissolved in absolute methyl alcohol (13 ml.), treated with redistilled pantolactone (2 equivs.; 11·1 g.), and refluxed for 1 hour with exclusion of moisture. After cooling, the almost clear solution was filtered, evaporated in a vacuum to constant weight, and sealed up in ampoules. A Van Slyke estimation indicated the presence of 0·8% of amino-nitrogen, corresponding to 90% condensation. The syrupy disulphide (1 g.) partly crystallised after 3 months. The semi-solid mass was digested with acetone and filtered quickly, without exposure to the air. After washing with dry acetone and finally with absolute ether, a white crystalline mass was obtained (400 mg.), m. p. 128—132°. It was dissolved in a large volume of boiling acetone (redistilled over potassium permanganate), and the filtered solution evaporated to small bulk and seeded. After 2 days' standing at 0°, the crystalline *bis-*(N-*pantoyl-β-aminoethyl*) *disulphide* was collected and washed with acetone and ether; it was no longer hygroscopic. Yield 160 mg., m. p. 140—142°. For analysis it was recrystallised again from acetone; m. p. 141—144° (Found: C, 46·1; H, 7·9; N, 6·2. $C_{16}H_{32}O_6N_2S_2$ requires C, 46·6; H, 7·8; N, 6·8%). For permanganate titration, see under bis-(*N*-pantoyl-β-aminoethyl) sulphoxide.

*Bis-β-aminoethyl Sulphide* (XII).—This was prepared, according to Mills and Bogert (*loc. cit.*), in 65% yield, b. p. 118—120°/17 mm. Permanganate titration (·S· ⟶ ·$SO_2$·) showed the purity to be 99%. The benzoyl derivative had m. p. 106—107° (Gabriel, *loc. cit.*, gives 106°).

*Bis-*(N-*pantoyl-β-aminoethyl*) *Sulphide* (V).—Bis-β-aminoethyl sulphide (2 g.) and redistilled pantolactone (4·3 g.) were dissolved in absolute methyl alcohol (4 ml.) and, after 12 hours, refluxed for 1 hour with exclusion of moisture. The solvent was evaporated in a vacuum at 40°, leaving a viscous oil. It was extracted twice with absolute ether to remove traces of unchanged aminoethyl sulphide, and a portion was then titrated in 50% acetic acid with permanganate; the result indicated a purity of 100%. A Van Slyke estimation showed the presence of 0·6% of amino-nitrogen, equivalent to 14% of unchanged bis-β-aminoethyl sulphide, *i.e.*, 86% condensation.

*Bis-β-aminoethyl Sulphoxide* (XIII).—A solution of bis-β-aminoethyl sulphide (1·2 g.) in water (10 ml.) was cooled to 0°, and bromine water added gradually until a slight permanent yellow colour remained. The solution was at once distilled in a vacuum, being kept cold until all bromine had been removed. The concentrated residue, while still warm, was treated at once with boiling absolute alcohol (10 ml.). The *sulphoxide dihydrobromide* crystallised in fine needles (2·82 g.; 97%). For recrystallisation it was dissolved in the minimum amount of warm water, and hot ethyl alcohol added until cloudiness just appeared; m. p. 201—202° (Found: N, 9·1; S, 10·5; Br, 54·4. $C_4H_{12}ON_2S,2HBr$ requires N, 9·4; S, 10·7; Br, 53·7%). Permanganate titration (·SO· ⟶ ·$SO_2$·) showed the purity to be *ca.* 100%.

The dihydrobromide (2·98 g.) was dissolved in water (5 ml.), and sodium ethoxide (2 equivs.; 0·46 g. of sodium in 20 ml. of absolute alcohol) added. The solvent was evaporated in a vacuum at 40°. Repeated addition of absolute alcohol and toluene (*ca.* 10 ml.), followed by evaporation in a vacuum, removed the last traces of water. Alcohol was then added, and sodium bromide (1·1 g.) removed. The filtrate was treated gradually with absolute ether (2 vols.) and kept until the precipitate had coagulated. Sodium bromide was again removed (total, 1·85 g.; theo., 2·06 g.). The filtrate, evaporated to dryness in a vacuum at 40°, left a syrupy residue (1·55 g.; theo., 1·36 g.).

This oil (117 mg.) was dissolved in ethyl alcohol (2 ml.) and treated with alcoholic hydrogen chloride; 160 mg. of aminoethyl sulphoxide dihydrochloride (theo., 178 mg.), m. p. 220°, were obtained. Permanganate titration of the free base in aqueous acetic acid indicated that the product was 97% pure.

*Bis-*(N-*pantoyl-β-aminoethyl*) *Sulphoxide* (VI).—Bis-β-aminoethyl sulphoxide (1·5 g.) and redistilled pantolactone (2·6 g.; 2 mols.) were dissolved in absolute methyl alcohol (4 ml.) and kept at 20° for 3 days. The slightly cloudy solution was filtered, and the solvent removed in a vacuum at 40°. The syrup obtained (4·1 g.) was sealed up in absence of air. Permanganate titration in aqueous acetic acid indicated the addition of 1·2 atoms of oxygen. On the assumption that this increased titre corresponds to a partial fission of the sulphoxide, as already discussed, the amount of sulphoxide in the mixture is *ca.* 92%. A Van Slyke determination showed 0·6% of amino-nitrogen, indicating 93% conversion.

*Isolation of Bis(pantoylaminoethyl) Disulphide* (IV) *from partly Crystalline Bis(pantoylaminoethyl) Sulphoxide Syrup.*—The partly crystalline syrup (7 g.) (prepared by refluxing the components together for 1 hour, evaporating the solvent in a vacuum, and keeping the residual syrup in a sealed tube for 3 months) was digested with acetone (dried, and redistilled over potassium permanganate). After filtration and washing with acetone and absolute ether, the crystals (2·6 g.) had m. p. 129—133° (to an opaque liquid). After recrystallisation from acetone, as described under the disulphide, they had m. p. 141—143°, raised after one more recrystallisation to 143—144° (sharp, to a clear liquid), not depressed by bis(pantoylaminoethyl) disulphide (Found: C, 47·0; H, 7·9; N, 6·8; S, 14·8. Calc. for $C_{16}H_{32}O_6N_2S_2$: C, 46·6; H, 7·8; N, 6·8; S, 15·5%). Permanganate titration of this crystalline material in glacial acetic acid represented an uptake of about 4·1 atoms of oxygen, the disulphide requiring 4 atoms of oxygen.

*Bis-β-aminoethylsulphone Dihydrochloride.*—(a) *Preparation from the sulphoxide.* 3% Potassium permanganate solution (1 equiv.) was added gradually to an ice-cold solution of the sulphoxide dihydrochloride (500 mg.) in 50% acetic acid (1 ml.). After decoloration with sulphur dioxide the solvent was evaporated in a vacuum. The solid residue was digested with absolute alcohol, excess of 10% alcoholic ammonia added, the inorganic salts removed and re-extracted three times with boiling alcohol, and the united extracts and filtrate evaporated to dryness in a vacuum; the residue was freed from traces of inorganic salts by repeated treatment with alcohol. The filtrate was treated with excess of alcoholic hydrogen chloride, and the precipitate collected and washed with alcohol and ether; needles (200 mg.) were

obtained, m. p. 226—228° after recrystallisation from 90% alcohol (Found: C, 21·5; H, 6·4; N, 12·6; S, 14·1; Cl, 31·1. $C_4H_{12}O_2N_2S,2HCl$ requires C, 21·3; H, 6·3; N, 12·4; S, 14·2; Cl, 31·5%).

(b) *Preparation from the sulphide.* Bis-β-aminoethyl sulphide (18 g.), dissolved in 180 ml. of 50% acetic acid, was cooled to 0°, and potassium permanganate (4 equivs.; 20·7 g. as a 3% solution in 50% acetic acid) added dropwise. The mixture was worked up as described under (a). The crude aminoethylsulphone dihydrochloride (29·7 g.), recrystallised from aqueous alcohol, gave needles (8·92 g.), m. p. 225—226°, not depressed by the *dihydrochloride* obtained under (a). Addition of alcohol to the filtrate gave a second crop (4·84 g.), m. p. 215°. A mixture of rosettes and needles (4 g.), m. p. 203°, obtained by concentrating the mother-liquors and adding more alcohol, was clearly a mixture; the nature of the impurity was not investigated. Only the high-melting material was used for condensations. The total yield was therefore only *ca.* 50%.

*Bis-(N-pantoyl-β-aminoethyl)sulphone.*—Bis-β-aminoethylsulphone (3·86 g.) (prepared from the dihydrochloride) and pantolactone (2 equivs.; 6·62 g.) were dissolved in absolute methyl alcohol (8 ml.), refluxed for 1 hour with exclusion of moisture, and left overnight at 20°. Evaporation of the solvent in a vacuum left a syrup (10·4 g.) which has not yet crystallised. Van Slyke determination showed 0·19% of free amino-nitrogen, which represents 97% condensation.

For *in vivo* tests, about 30 g. of each of the above analogues were prepared.

Microanalyses were carried out by Drs. Weiler and Strauss of Oxford.

The author is grateful to Mr. F. A. Robinson for the suggestion to undertake the preparation of the above series of compounds, and for much helpful advice, and to Dr. J. Ungar of the Department of Experimental Medicine, Glaxo Laboratories, Ltd., for carrying out the animal tests. The author also wishes to express her indebtedness to Miss H. Weil and Miss B. M. Wilson for valuable assistance throughout the investigation.

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## 4. *Preparation of 6-Nitro-1-naphthol, Improved Methods for the Decomposition of Diazo-naphthols, and New Reactions of Nitronaphthols.*

By HERBERT H. HODGSON and HAROLD S. TURNER.

6-Nitro-1-naphthol, 6-bromo-1-naphthol, and 4 : 5-dinitro-2-naphthol have been prepared from the corresponding diazonaphthols by improved methods of decomposition. The electronic effect of the 6-nitro-group on position 2 is greater than that of the 6-bromo-substituent. 2 : 4-*Dibromo-6-nitro-1-naphthol* has been obtained from one molecule each of bromine and 6-nitro-2-diazo-1-naphthol. Monobromination and monomercuration of 6-nitro-1-naphthol occur in position 4.

THE replacement of diazo-nitrogen in a diazo-naphthol by hydrogen by Morgan and Evens's method (J., 1919, **115**, 1126) is accomplished by boiling with ethyl alcohol in the presence of a metallic powder or hypophosphorous acid. The reaction is very slow; *e.g.*, 4-nitro-1-diazo-2-naphthol requires 32 hours with aluminium powder. When precipitated copper is added, however, the time is reduced to 12 hours and the yield (45—50%) is larger than that obtained (38%) when aluminium is used alone. Similarly, 4 : 5-*dinitro-1-diazo-2-naphthol* is readily reduced by the copper–aluminium mixture.

The decomposition of 6-nitro-2-diazo-1-naphthol could not be effected by Morgan and Evens's method even after 34 hours' boiling, but was accomplished in 30 minutes when its solution in glacial acetic–concentrated sulphuric acid was added to a suspension of yellow precipitated cuprous oxide in ethyl alcohol (cf. Hodgson and Turner, J., 1943, 86).

6-Nitro-2-diazo-1-naphthol is also non-reactive towards concentrated aqueous potassium iodide, even when cuprous iodide is added, and towards a suspension of cuprous iodide in hydriodic acid, but reacts immediately when its solution in glacial acetic–sulphuric acid is added to a suspension of precipitated copper powder in saturated aqueous potassium iodide: the reactivity may be due to the diazonium salt re-formed by the sulphuric acid. In a neutral or a weakly acid medium (ethyl alcohol and acetic acid) this diazo-oxide is stable towards the usual reagents for diazo-compounds.

In the preparation of 6-*bromo-2-diazo-1-naphthol*, *p*-toluenesulphon-2-naphthalide is brominated in glacial acetic acid at 90—100°; after the mixture of 1 : 6-dibromo-*p*-toluenesulphon-2-naphthalide and 1 : 6-dibromo-2-naphthylamine hydrobromide obtained has been basified, hydrolysed, and diazotised in sulphuric–glacial acetic acid, the removal of mineral acid by sodium acetate brings about the formation of the diazo-oxide in 84·5% yield.

6-Nitro-1-naphthol, hitherto difficultly accessible (cf. Veselý and Dvorák, *Bull. Soc. chim.*, 1923, **33**, 319), has now been prepared in good yield from 6-nitro-2-diazo-1-naphthol, itself readily obtained from 1 : 6-dinitro-*p*-toluenesulphon-2-naphthalide (Hodgson and Turner, *loc. cit.*).

The reaction between equivalent amounts of bromine and 6-nitro-2-diazo-1-naphthol produces 2 : 4-*dibromo-6-nitro-1-naphthol* without evolution of hydrogen bromide, possibly as follows:

$$NO_2\cdot C_{10}H_5\!\!<\!\!\begin{matrix}O\\|\\N_2\end{matrix} \xrightarrow{2\,Br_2} NO_2\cdot C_{10}H_4Br(OH)\cdot N_2Br_2 \longrightarrow NO_2\cdot C_{10}H_4Br_2\cdot OH + Br_2 + N_2$$

6-Nitro-1-naphthol is monobrominated and monomercurated in position 4, like 6-nitro-1-naphthylamine (Hodgson and Turner, J., 1943, 391). The *mercuriacetate* is readily converted into 4-*iodo-6-nitro-1-naphthol*. The 4-halogeno-derivatives were oriented by their difference from the only possible alternatives, the 2-halogeno-derivatives, which were synthesised from 6-nitro-2-diazo-1-naphthol.

## Experimental.

All m. p.'s are corrected.

*6-Nitro-2-diazo-1-naphthol.*—1 : 6-Dinitro-*p*-toluenesulphon-2-naphthalide (50 g.) was hydrolysed and diazotised (Hodgson and Turner, this vol., p. 86), and the diazonium solution poured into ice-water (6 l.). After 12 hours, the diazonaphthol was collected, washed with water, and dried at 60°; yield, 26·6 g. (95·5%). It crystallised from glacial acetic acid in yellow-brown needles, which exploded at 150—151° (Gaess and Ammelburg, *Ber.*, 1894, **27**, 2211, give expl. p. 142—145°; Scheid, *Ber.*, 1901, **34**, 1816, gives 151—157°) (Found : N, 19·6. Calc. : N, 19·5%).

*6-Nitro-1-naphthol.*—The above diazo-naphthol (10 g.) was dissolved in a mixture of glacial acetic acid (75 c.c.) and sulphuric acid (75 c.c., *d* 1·84) below 20°, and the solution added during 15 minutes to a well-stirred suspension of precipitated cuprous oxide (25 g.) in alcohol (200 c.c.), initially at 55°; nitrogen was evolved and the temperature rose to 82°. A further quantity (7 g.) of cuprous oxide was then added, and stirring continued at 80° for 30 minutes. The solid was collected and washed with a little boiling alcohol and the combined filtrate and washings were stirred into a mixture of ice and water (1 l.). After 12 hours, the precipitate was collected and dissolved in warm 2% aqueous sodium hydroxide (200 c.c.), the deep red solution filtered and acidified with dilute hydrochloric acid, and the precipitated 6-nitro-1-naphthol (5·2—6·0 g.; 60—70% yield) collected, washed, dried, and crystallised from glacial acetic acid, forming yellow elongated plates, m. p. 181—182° (Veselý and Dvorák, *loc. cit.*, give m. p. 179°) (Found : N, 7·5. Calc : N, 7·4%).

*6-Nitro-1-naphthyl acetate*, formed from 6-nitro-1-naphthol (1·0 g.) in boiling acetic anhydride (5 c.c.) and glacial acetic acid (5 c.c.), crystallised from dilute acetic acid (charcoal) in slender cream needles, m. p. 121° (Found : N, 6·3. $C_{12}H_9O_4N$ requires N, 6·1%). *6-Nitro-1-naphthyl benzoate*, prepared by the Schotten–Baumann method, crystallised from ethylene dichloride in cream needles, m. p. 147·5—148° (Found : N, 4·6. $C_{17}H_{11}O_4N$ requires N, 4·8%).

*2-Chloro-6-nitro-1-naphthol.*—The paste made from 6-nitro-2-diazo-1-naphthol (2·0 g.), hydrochloric acid (20 c.c., *d* 1·16), water (10 c.c.), and cuprous chloride (2·0 g.) was heated on the water-bath until nitrogen ceased to be evolved (2 hours). After dilution with water, the solid (2·1 g.) was collected, washed with dilute hydrochloric acid and with water, and dried. *2-Chloro-6-nitro-1-naphthol* crystallised from glacial acetic acid in chrome-yellow needles, m. p. 179—180°) (Found : N, 6·5. $C_{10}H_6O_3NCl$ requires N, 6·3%).

*2-Chloro-4-bromo-6-nitro-1-naphthol* was formed when 2-chloro-6-nitro-1-naphthol (0·95 g.), dissolved in glacial acetic acid (20 c.c.), was treated with a 25% (w./v.) solution of bromine in glacial acetic acid (2·8 c.c.) at 60°, the mixture heated at 90° for 5 minutes, and the volume then reduced to 10 c.c.; on cooling, primrose-yellow needles separated, m. p. 199° and after recrystallisation from glacial acetic acid (Found : N, 5·0. $C_{10}H_5O_3NClBr$ requires N, 4·7%).

*2-Bromo-6-nitro-1-naphthol* was formed when 6-nitro-2-diazo-1-naphthol (5·0 g.) was added to a solution of cuprous bromide (5·0 g.) in hydrobromic acid (50 c.c., 30%) and the mixture heated on the water-bath for 4 hours. 5% Hydrochloric acid was added, and the bromonitronaphthol (7·2 g.) crystallised from 70% acetic acid (charcoal), forming mustard-yellow needles, m. p. 164·5—165·5° (Found : N, 5·4. $C_{10}H_5O_3NBr$ requires N, 5·2%).

*4-Bromo-6-nitro-1-naphthol* was obtained when a solution of 6-nitro-1-naphthol (6·2 g.) in glacial acetic acid (40 c.c.) was shaken with a mixture of glacial acetic acid (10 c.c.) and a 20% solution of bromine in glacial acetic acid (8·5 c.c.), added gradually. After 2 hours, the solution was heated on the water-bath for 1 hour, evaporated to small bulk with charcoal, filtered, and allowed to crystallise; the bromonitronaphthol crystallised from 80% acetic acid in orange needles, m. p. 238° (Found : N, 5·5. $C_{10}H_5O_3NBr$ requires N, 5·2%).

*2 : 4-Dibromo-6-nitro-1-naphthol* was formed when 6-nitro-1-naphthol (1 g.), dissolved in glacial acetic acid (15 c.c.), was heated on the water-bath for 30 minutes with the above solution of bromine (8·5 c.c.); after concentration to 10 c.c. (charcoal) and filtration, the filtrate deposited the dibromonitronaphthol in greenish-yellow needles, m. p. 210° after recrystallisation from glacial acetic acid (Found : N, 4·2. $C_{10}H_4O_3NBr_2$ requires N, 4·0%). Alternatively, 6-nitro-2-diazo-1-naphthol (5·0 g.), dissolved in glacial acetic acid (65 c.c.) at 110°, was shaken with a solution of bromine (1·2 c.c.) in glacial acetic acid (3 c.c.), nitrogen only being evolved. The dibromonitronaphthol (5·1 g.) separated on cooling; recrystallised from glacial acetic acid, it formed greenish-yellow needles, m. p. and mixed m. p. 210° (Found : N, 4·2%).

*2-Iodo-6-nitro-6-naphthol.*—A solution of 6-nitro-2-diazo-1-naphthol (2·6 g.) in a cold mixture of glacial acetic acid (15 c.c.) and sulphuric acid (15 c.c., *d* 1·84) was stirred into aqueous potassium iodide (30 g. in 25 c.c.) at 95° in which copper powder (4·0 g.) was suspended. When the vigorous evolution of nitrogen had ceased, the mixture was diluted to 150 c.c., aqueous sodium thiosulphate added to remove free iodine, and the solid collected, washed with water, dried, and extracted with boiling acetone (50 c.c.). The extract afforded *2-iodo-6-nitro-1-naphthol* (1·4 g.), which crystallised from glacial acetic acid (charcoal) in brass-yellow elongated plates, m. p. 214—215° (decomp. and evolution of iodine after discoloring above 200°) (Found : N, 4·5. $C_{10}H_5O_3NI$ requires N, 4·45%).

*6-Nitro-1-naphthol-4-mercuriacetate* was obtained when a mixture of 6-nitro-1-naphthol (3·0 g.), glacial acetic acid (20 c.c.), and mercuric acetate (6·0 g.) was boiled to effect solution, heated on the water-bath for 1 hour, and kept overnight. The dense, yellow, crystalline solid (5·4 g.) which separated was washed with glacial acetic acid and alcohol, dried, and recrystallised from glacial acetic acid, forming cream-coloured, almost colourless, lustrous, feathery needles, m. p. above 360° (shrinking at 300°) (Found : Hg, 44·1. $C_{12}H_9O_5NHg$ requires Hg, 44·7%).

*4-Iodo-6-nitro-1-naphthol.*—The above mercuriacetate (1·8 g.), suspended in 20% aqueous potassium iodide (20 c.c.) at 90°, was heated with a solution of iodine (0·92 g.) in hot 30% aqueous potassium iodide for 5 minutes on the water-bath, the mixture cooled and treated with sodium thiosulphate, and the *4-iodo-6-nitro-1-naphthol* crystallised from glacial acetic acid, forming light brownish-yellow needles, m. p. 214—216° (without noticeable decomp.; cf. the 2-iodo-isomeride above); mixed m. p. with 2-iodo-6-nitro-1-naphthol, 192—198° (Found : N, 4·4. $C_{10}H_5O_3NI$ requires N, 4·45%).

*4 : 5-Dinitro-1-diazo-2-naphthol.*—2 : 4 : 5-Trinitro-*p*-toluenesulphon-1-naphthalide (7·2 g.) (Hodgson and Turner, J., 1942, 724) was dissolved in sulphuric acid (20 c.c., *d* 1·84), below 20°, mixed with a solution of sodium nitrite (2·0 g.) in sulphuric acid (15 c.c., *d* 1·84), and stirred into glacial acetic acid (40 c.c.) below 20°. After 1 hour the diazo-solution was run into ice-water (1 l.), and a slight excess of sodium acetate added to neutralise the free sulphuric acid. After 12 hours, the *4 : 5-dinitro-1-diazo-2-naphthol* (4·2 g.; 97%) was removed, washed, and dried in a vacuum; it crystallised from glacial acetic acid in yellow needles, which decomposed slowly when heated gradually, but exploded at 160° when heated rapidly (Found : N, 21·3. $C_{10}H_4O_5N_4$ requires N, 21·5%).

*4 : 5-Dinitro-2-naphthol.*—When the above diazo-naphthol (1 g.) in alcohol (25 c.c.) was refluxed with aluminium powder (0·2 g.) on a water-bath for 4 hours (cf. Morgan and Evens, *loc. cit.*), little reaction occurred, but when precipitated copper (0·05 g.) was added, the rate of decomposition was greatly accelerated and, after refluxing for a further 2½ hours, the solution gave no coupling colour with alcoholic alkaline resorcinol. After filtration, the pale purple filtrate was evaporated to dryness on the water-bath, and the residue extracted repeatedly with boiling water (in 60 c.c. portions). 4 : 5-Dinitro-2-naphthol, which crystallised from the combined extracts on cooling, separated from 50% aqueous alcohol in deep yellow, micro-lenticular crystals, m. p. 237—238° (Bell, J., 1933, 288, gives m. p. *ca.* 230°) (Found : N, 12·1. Calc. : N, 11·95%).

*1-Bromo-4 : 5-dinitro-2-naphthol* was formed when 4 : 5-dinitro-1-diazo-2-naphthol (1·0 g.), made into a paste with hydrobromic acid (5 c.c., 30%), was treated with a solution of cuprous bromide (2·0 g.) in hydrobromic acid (10 c.c., 30%)

and heated on the water-bath for 2 hours. After dilution with water, the bromodinitronaphthol was collected, washed, dried, and twice crystallised from dilute acetic acid, forming light lemon-yellow needles, m. p. 218—220° (Found : N, 9·3. $C_{10}H_5O_5N_2Br$ requires N, 9·4%).

6-*Bromo*-2-*diazo*-1-*naphthol*.—A solution of *p*-toluenesulphon-2-naphthalide (40 g.) in glacial acetic acid (100 c.c.) was treated at 90° with one of bromine (13·6 c.c.) in glacial acetic acid (50 c.c.). After 5 minutes the pasty mass of cream needles was cooled, washed, after filtration, with a little glacial acetic acid, and dried in a vacuum. The product was suspended in water and rendered faintly alkaline with dilute sodium carbonate solution, and the solid was collected, washed, dried in a vacuum, dissolved in cold sulphuric acid (90 c.c., *d* 1·84) and treated with a solution of sodium nitrite (9·0 g.) in sulphuric acid (65 c.c., *d* 1·84). The diazo-solution was stirred into glacial acetic acid (220 c.c.) below 20°, and the mixture added after 30 minutes to ice-water (6 l.) containing sufficient sodium acetate to neutralise the mineral acid. After 14 days the precipitate (18·5 g.) of 6-*bromo*-2-*diazo*-1-*naphthol* was collected, washed, and dried in a vacuum; it crystallised from glacial acetic acid in stout brownish needles and from acetone in slender, matted, yellow needles, m. p. 214° (decomp.) after darkening at about 145° and shrinking at about 160° (Found : N, 11·2. $C_{10}H_5ON_2Br$ requires N, 11·2%).

6-*Bromo*-1-*naphthol*.—A mixture of the above diazo-naphthol (10 g.), alcohol (125 c.c.), aluminium powder (1·0 g.), copper powder (1·0 g.), and Devarda's alloy (4·0 g.) was refluxed for 10½ hours. After filtration, the liquid was evaporated to dryness on the water-bath, and the residue boiled repeatedly with water until the filtered extracts no longer deposited 6-bromo-1-naphthol on cooling. The colourless needles obtained had m. p. 128·5—129·5° (Fuson, *J. Amer. Chem. Soc.*, 1925, **47**, 516, gives m. p. 129—130°).

1 : 6-*Dinitronaphthalene*-2-*azo*-β-*naphthol* was obtained when 1 : 6-dinitro-*p*-toluenesulphon-2-naphthalide (5·0 g.) was hydrolysed and diazotised as above, and the diazo-solution diluted with ice-water (100 c.c.) and added *at once* to a solution of β-naphthol (1·9 g.) in 20% aqueous sodium hydroxide (100 c.c.) and water (100 c.c.) below 10°. The precipitated, washed, and dried dye crystallised from tetrachloroethane in deep red, prismatic needles, m. p. 310° (Found : N, 14·3. $C_{20}H_{12}O_5N_4$ requires N, 14·4%); it also crystallised readily from nitrobenzene, ethylene dichloride, chloroform, tetralin, pyridine, and diethylaniline.

The authors thank I.C.I. (Dyestuffs) Ltd. for gifts of chemicals.

TECHNICAL COLLEGE, HUDDERSFIELD. [*Received, July 22nd*, 1943.]

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## 5. *Decomposition of Diazotised* 1 : 6-*Dinitro*-2-*naphthylamine by Precipitated Copper in Organic Solvents.*

By HERBERT H. HODGSON and HAROLD S. TURNER.

Precipitated copper deaminates 1 : 6-dinitro-2-naphthylamine without the induction period observed when cuprous oxide is used (J., 1943, 86), and in the case of methyl alcohol without production of formaldehyde. The yields obtained by both procedures are similar with methyl, ethyl, and *iso*propyl alcohol, but not with ethylene chlorohydrin.

Some comparative deaminations of 2-nitro-1-naphthylamine are included.

PREVIOUS work (J., 1942, 748; 1943, 86) on the action of cuprous oxide on diazotised amines in various media has been supplemented by an examination of the reaction of precipitated copper under the same conditions with diazotised 1 : 6-dinitro-2-naphthylamine. The copper dissolved, and, in general, where an alcohol was the solvent, oxidation to the corresponding aldehyde occurred. Methyl alcohol did not give rise to formaldehyde, nevertheless the yield of deaminated product (*ca.* 58%) was almost the same as that obtained with cuprous oxide (*ca.* 60%) (in this reaction formaldehyde is produced), so methyl alcohol again heads the list of alcohols arranged in order of decreasing efficiency. Since oxidation must occur as a complement to reduction of the diazo-compound, methyl alcohol must have been oxidised to carbon dioxide, because the formation of formic acid was never detected.

When the diazonium solution prepared in glacial acetic–sulphuric acid was decomposed in the absence of any other solvent, the amount of deamination was almost negligible (10%), and in this case, as also when methyl, ethyl, *n*-propyl, *iso*propyl, *n*-butyl, β-chloroethyl alcohol, acetone, methyl ethyl ketone, ethyl formate, or ethyl acetate was present, there was no induction period before the evolution of nitrogen (cf. Hodgson and Turner, J., 1943, 86); deamination in presence of *n*-propyl, *iso*propyl, or *n*-butyl alcohol, however, was somewhat sluggish. A short induction period was observed with *iso*butyl alcohol and a slightly longer one with amyl alcohol. Generally, it was necessary to pass steam into the diluted reaction mixture to remove alcohols or esters immiscible with water. Ethyl acetate and amyl alcohol produced tars; with ethyl formate very little gas was evolved and the reaction mixture on dilution did not give a solid precipitate, although there was the normal rise in temperature during the reaction.

The yields obtained with precipitated copper are slightly lower than those with cuprous oxide, and ethylene chlorohydrin is no longer the most efficient deaminating solvent, its place being taken by methyl alcohol.

Deaminations were also carried out with diazotised 2-nitro-1-naphthylamine in methyl, ethyl, and β-chloroethyl alcohol. The order of yields was the same as with 1 : 6-dinitro-2-naphthylamine, *viz.*, methyl > ethyl > β-chloroethyl alcohol, but the amounts were smaller than those given by the cuprous oxide procedure.

### EXPERIMENTAL.

*Precipitated Copper*.—Copper was precipitated from copper sulphate solution with zinc dust, washed with water, stirred with dilute hydrochloric acid to remove zinc, washed with alcohol and ether, and stored in a stoppered bottle slightly wetted with ether.

*Procedure.*—The diazonium salt solution was prepared from 1 : 6-dinitro-*p*-toluenesulphon-2-naphthalide (20 g.) by combined hydrolysis and diazotisation (J., 1943, 88) and poured into a suspension of copper powder in the organic solvent (200 c.c.) at 15°. Details are given in the Table.

*Deamination by Copper Powder.*

| Medium (200 c.c.). | Copper, g. | Max. temp. | Yield, g. | Yield, %. | M. p. | Description of product. | Remarks. |
|---|---|---|---|---|---|---|---|
| None | 20 | 56° | 1·2 | 10·5 | 163 —164° | Brown needles | (1) |
| Methyl alcohol | 20 | 65 | 6·55 | 58 | 165·5—166·5 | Yellow needles | (1) |
| Ethyl alcohol | 12 | 65 | 6·5 | 57·5 | 165·5—166·5 | Yellow needles | (1) |
| *iso*Propyl alcohol | 25 | 65 | 6·1 | 54·5 | 164·5—165·5 | Light yellow needles | (1) Reaction sluggish |
| *n*-Propyl alcohol | 20 | 70 | 4·0 | 35·5 | 163·5—165·5 | Yellow needles | (1) Slow reaction |
| *iso*Butyl alcohol | 25 | 58 | 2·9 | 26 | 163·5—164·5 | Golden-brown needles | (2) Slow reaction |
| *n*-Butyl alcohol | 20 | 66 | 4·1 | 36·5 | 163·5—165 | Golden-brown needles | (1) Slow reaction |
| β-Chloroethyl alcohol | 30 | 50 | 4·0 | 36 | 163 —165 | Light brown needles | (1) |
| Acetone | 20 | 60 | 1·8 | 16 | 123 —133 | Deep brown needles | (1) |
| Methyl ethyl ketone | 20 | 65 | 5·0 | 44·5 | 161·5—162·5 | Golden-brown needles | (1) |
| Ethyl formate | 30 | 36 | — | — | — | Water-soluble product | (1) Slight effervescence |
| Ethyl acetate | 30 | 51 | — | — | — | Tar | (1) |
| Amyl alcohol | 30 | 59 | — | — | — | Tar | (3) |

(1) No induction period. (2) Small induction period. (3) Induction period while temperature rose to 30°.

*Deamination of 2-Nitro-1-naphthylamine* —Solutions of the amine (9·4 g.) in sulphuric acid (50 c.c., *d* 1·84) and of sodium nitrite (4·5 g.) in sulphuric acid (30 c.c., *d* 1·84) were mixed in the cold and added below 20° to glacial acetic acid (100 c.c.). The diazo-solution was stirred into a suspension of copper powder (20 g.) in the alcohol (120 c.c.) at 15°; after the reaction was completed, the mixture was steam-distilled, and the 2-nitronaphthalene collected.

| Medium. | Maximum temperature. | Yield. G. | Yield. %. |
|---|---|---|---|
| Methyl alcohol | 65° | 3·0 | 35 |
| Ethyl alcohol | 60 | 2·9 | 33·5 |
| Ethylene chlorohydrin | 60 | 2·25 | 26 |

The authors thank I.C.I. (Dyestuffs) Ltd. for gifts of chemicals.

TECHNICAL COLLEGE, HUDDERSFIELD. [*Received, July 22nd,* 1943.]

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## 6. *Reactions of Benzthiazole Derivatives. Part IV.* 1-*Thiocyanobenzthiazole.*

By W. H. DAVIES and W. A. SEXTON.

1-Thiocyanobenzthiazole is readily converted by many reagents into derivatives of 1-thiolbenzthiazole. With alcohols, however, it gives the thioncarbamates derived from 1-aminobenzthiazole. The mechanism of this is discussed.

WHEN alcoholic potassium thiocyanate was heated with 1-chlorobenzthiazole, approximately the theoretical amount of potassium chloride was precipitated but only a small amount of the expected 1-thiocyanobenzthiazole was isolated. This thiocyano-compound was therefore prepared from cold alcoholic sodio-1-thiolbenzthiazole and cyanogen bromide (Levi, *Gazzetta*, 1931, **61**, 383). The yield was excellent and the crude product could readily be purified by crystallisation from ether, but attempted crystallisation from hot alcohols, as recommended by Levi, gave mixtures containing a considerable amount of higher-melting material. These unexpected results led us to investigate more closely the stability of 1-thiocyanobenzthiazole to heat and to chemical reagents.

1-Thiocyanobenzthiazole is not stable to prolonged storage and decomposes fairly rapidly on heating. With aqueous sodium hydroxide and sulphide, sodio-1-thiolbenzthiazole was formed in good yield. With sodium methoxide in methyl alcohol, a vigorous reaction gave sodio-1-thiolbenzthiazole, sodium cyanate, and 1-methylthiobenzthiazole. Similarly, sodium ethoxide in ethyl alcohol gave the same sodium salts, together with 1-ethylthiobenzthiazole. Analogous sulphides have been reported from the reaction between thiocyanobenzene and sodium ethoxide (Ross, *J. Amer. Chem. Soc.*, 1934, **56**, 727), and the formation of cyanate was observed by Levi (*loc. cit.*) in the reaction between dibenzthiazyl disulphide and excess of alcoholic potassium cyanide.

When 1-thiocyanobenzthiazole was heated in benzene or, better, toluene, an orange amorphous precipitate (presumably " pseudocyanogen sulphide "; see, *e.g.*, Wheeler and Johnson, *J. Amer. Chem. Soc.*, 1902, **24**, 680) was formed and from the solution dibenzthiazyl monosulphide was isolated; there was no evidence of the formation of an *iso*thiocyano-compound. With a benzene suspension of sodio-1-thiolbenzthiazole, the same products were obtained, together with a small amount of dibenzthiazyl disulphide. The yield of monosulphide was, however, much higher in this case, and this fact, together with the qualitative detection of SCN′ in the product, indicates that some of the monosulphide was derived by direct action of the thiocyano-compound with the sodio-derivative with elimination of sodium thiocyanate. In this case, the SCN group is functioning as a pseudo-halogen.

When 1-thiocyanobenzthiazole was heated in alcohol, no trace of " pseudocyanogen sulphide " was observed.

With methyl alcohol, a small amount of dibenzthiazyl disulphide was isolated, but the main product was *methyl benzthiazyl-1-thioncarbamate*, which was characterised by analysis, solubility in alkali, stability to dilute alkali and acid, and hydrolysis with strong acid to 1-aminobenzthiazole. Homologous derivatives were obtained with higher alcohols [Chi and co-workers (*J. Amer. Chem. Soc.*, 1930, **52**, 1580; 1932, **54**, 2056; 1933, **55**, 418) found that certain thiocyanopyrimidines react with alcohols to give thioncarbamates].

A possible mechanism for this reaction as well as for the formation of alkylthiobenzthiazoles in the reaction with sodium alkoxides might involve the formation of the unstable intermediate imino-thiocarbonic esters (I). [Although the formation of imino-ethers from nitriles and alcohols is usually carried out in the presence of an acid, the reversible addition of alcohols to nitriles with a sodium alkoxide catalyst is also well established (Marshall, jun., Acree, and co-workers, *Amer. Chem. J.*, 1913, **49**, 127, 369).] Such an imino-ether would be expected to lose cyanic acid and give the alkyl sulphide (II), this being analogous to the loss of cyanamide from the hypothetical intermediate (III) derived from thiourea and 1-chlorobenzthiazole (Scott and Watt, *J. Org. Chem.*, 1937, **2**, 148; Watt, *ibid.*, 1939, **4**, 436) and to the thermal decomposition of methyl iminodithiocarbonate [$NH{:}C(SMe)_2$] to methylthiol and methyl trithiocyanurate (Delépine, *Bull. Soc. chim.*, 1903, **29**, 55). Alternatively the imino-ether (I) might rearrange to give the thioncarbamate (IV), such migrations of a group from sulphur to nitrogen in the system $\cdot N{:}C\cdot SR$ having been previously reported (Reed, Robertson, and Sexton, J., 1939, 473).

$$\underset{\text{(II.)}}{HO\cdot CN} + R\cdot SR' \longleftarrow \underset{\text{(I.)}}{[RS\cdot C(:NH)\cdot OR']} \longrightarrow \underset{\text{(IV.)}}{NHR\cdot CS\cdot OR'}$$

$$R\cdot SH + NH_2\cdot CN + HCl \longleftarrow \underset{\text{(III.)}}{[RS\cdot C(:NH)\cdot NH_2,HCl]} \xrightarrow{RCl} R_2S + NH_2\cdot CN + 2HCl$$

R = 1-Benzthiazyl.

Little is known of the properties of iminothiocarbonates of type (I). Knorr (*Ber.*, 1916, **49**, 1735; 1917, **50**, 229, 767) prepared hydrochlorides in which R was alkyl, but the free bases were too unstable to be isolated and even the hydrochlorides, in the presence of water or an alcohol, decomposed to give the thiolcarbamates ($NH_2\cdot CO\cdot SR$) and an alkyl chloride. 1-Thiocyanobenzthiazole in excess of methyl alcohol was treated with hydrogen chloride; when the product was poured into water, 1-methylthiobenzthiazole was obtained in good yield but no 1-benzthiazyl thiolcarbamate, analogous to the products obtained from alkyl thiocyanates (Knorr, *loc. cit.*), was detected. This suggests that the mode of decomposition of the iminothiocarbonates differs, as might be expected, according to their substituents and that, in the case of the benzthiazyl derivative at least, decomposition by elimination of cyanic acid is possible.

If the mechanism suggested for these reactions is correct, it would imply that the formation of iminothiocarbonates from thiocyanates may be fairly general (cf. reactions with thiocyanobenzene; Ross, *loc. cit.*) but that the subsequent isomerisation to thioncarbamates is rarer, being dependent on the nature of the radical attached to the thiocyano-group.

## Experimental.

1-*Thiocyanobenzthiazole*.—A specimen prepared according to Levi (*loc. cit.*) and crystallised from ether had m. p. 87—88°.

*Stability*. (i) A sample stored in a glass vessel for 3½ years had become yellow and had m. p. 82—87° (softening at 77°).

(ii) Resinous material was formed on heating at 70° for 4 hours. In boiling benzene, an amorphous orange solid was precipitated during 48 hours. 1-Thiocyanobenzthiazole (1·92 g.) was heated in boiling toluene (50 c.c.) for 24 hours: the amorphous orange precipitate (0·49 g.) was removed, and the filtrate concentrated to yield, on cooling, dibenzthiazyl sulphide (0·94 g., 64%), m. p. 101° after crystallisation from alcohol, not depressed by an authentic specimen (Watt, *loc. cit.*).

*Reactions*. (i) *With sodium hydroxide*. 1-Thiocyanobenzthiazole (2·0 g.) and 2N-sodium hydroxide (10 c.c.) were stirred at 70—80° for 2 hours, cooled, and filtered. Addition of 2N-hydrochloric acid (10 c.c.) precipitated 1-thiolbenzthiazole (1·54 g., 88%). The filtrate contained sodium cyanate, which was indicated by evolution of carbon dioxide on acidification and the presence of ammonia in the acidified liquor.

(ii) *With sodium sulphide*. 1-Thiocyanobenzthiazole (3·84 g.) dissolved exothermally in the calculated quantity of aqueous sodium sulphide. On acidification, 1-thiolbenzthiazole (3·34 g., 100%) was precipitated, m. p. 177—178°.

(iii) *With alcoholic sodium methoxide*. 1-Thiocyanobenzthiazole (4·8 g.) was added during 10 minutes to a stirred solution of sodium methoxide (sodium, 0·6 g., in methyl alcohol, 30 c.c.) maintained at about 0°. After a further 15 minutes at 0°, the solution was filtered from sodium cyanate (0·62 g., 37·5%), poured into water, and separated into neutral and alkali-soluble fractions, from which were isolated 1-methylthiobenzthiazole (1·61 g., 35%), m. p. 38—43°, mixed m. p. with authentic material 39—45°, and 1-thiolbenzthiazole (2·37 g., 57%), m. p. and mixed m. p. with authentic material, 176—177°.

(iv) *With alcoholic sodium ethoxide*. This was carried out as for the methoxide reaction but at 10° instead of 0°. The products were sodium cyanate (0·46 g., 38%), 1-thiolbenzthiazole (2·48 g., 55%), and 1-ethylthiobenzthiazole (1·78 g., 42%).

(v) *With sodio-1-thiolbenzthiazole in methyl alcohol*. 1-Thiocyanobenzthiazole (3·84 g.) was added to a solution of sodio-1-thiolbenzthiazole (3·78 g.) in methyl alcohol (30 c.c.) with good stirring; the temperature rose slowly from 22° to 27°. After 2 hours' stirring, the precipitate (2·0 g.) of sodium cyanate and dibenzthiazyl disulphide was collected and washed with water to remove the cyanate; the residue was identified as the disulphide (1·26 g., 37·5%). The weight of sodium cyanate (identified in the filtrate by the usual tests) was therefore 0·74 g. (57%). The alcoholic filtrate was poured into water and separated with alkali to give 1-methylthiobenzthiazole (2·56 g.), m. p. 37—41°, and 1-thiolbenzthiazole (2·23 g.), m. p. and mixed m. p. with authentic material 175—177°.

(vi) *With sodio-1-thiolbenzthiazole in benzene*. 1-Thiocyanobenzthiazole (1·92 g.) and sodio-1-thiolbenzthiazole (1·89 g.) were heated in boiling benzene (50 c.c.) for 24 hours, and the solution filtered hot from the orange insoluble

material (1·8 g.). This orange product was extracted with water, and the extract acidified to precipitate 1-thiolbenzthiazole (0·6 g.), m. p. and mixed m. p. with authentic material, 176—178°: the aqueous filtrate gave qualitative reactions for $SCN'$. The benzene filtrate, on cooling, gave plates (0·3 g.), m. p., after crystallisation from benzene, 178—179°, alone or mixed with dibenzthiazyl disulphide. The benzene filtrate was evaporated to dryness to give a yellow solid (1·7 g.), m. p. 89—92°, which, after two crystallisations from alcohol to remove the sparingly soluble dibenzthiazyl disulphide, gave dibenzthiazyl monosulphide in pale yellow needles, m. p. 97—98°, not depressed by an authentic sample (m. p. 101°).

(vii) *With methyl alcohol.* 1-Thiocyanobenzthiazole (20 g.) was heated in boiling methyl alcohol (150 c.c.) for 24 hours, a further 350 c.c. of alcohol being added gradually to prevent separation of solid. After clarification with charcoal and cooling, crystals (6·0 g.) separated, m. p. 166—168°, raised by successive crystallisation from methyl alcohol, benzene, and light petroleum to 175°. From the original alcoholic mother-liquors, more of this material (crude) as well as dibenzthiazyl disulphide, m. p. and mixed m. p. with authentic material, 177—178°, were obtained. The new compound dissolved in dilute alkali solution and was precipitated unchanged on acidification. Heating for 2 hours with dilute alcoholic sodium hydroxide did not affect it, but boiling with 30% aqueous sodium hydroxide caused profound decomposition. The compound was also soluble in hot 36% hydrochloric acid. It resisted the action of 15% methyl-alcoholic sulphuric acid, but when the material (1 g.) was boiled for 1 hour with 5% sulphuric acid (14 g.) a white solid separated. This was dissolved by addition of water and a base was precipitated on addition of alkali. The base (0·45 g.), m. p. 126—128°, was identified as 1-aminobenzthiazole by mixed m. p. with authentic material and by its characteristic colour reactions with hypochlorite and sulphuric acid. On the basis of these reactions, the methyl alcohol reaction product is identified as *methyl benzthiazyl-1-thioncarbamate* (Found: C, 48·5; H, 3·4; N, 12·5; S, 27·9. $C_9H_{10}ON_2S_2$ requires C, 48·2; H, 3·6; N, 12·5; S, 28·6%).

(viii) *With other alcohols.* With ethyl alcohol, 10 hours' heating sufficed to convert 1-thiocyanobenzthiazole into *ethyl benzthiazyl-1-thioncarbamate*, m. p. 163° after crystallisation from alcohol (Found: C, 50·2; H, 4·5; N, 12·1; S, 27·0. $C_{10}H_{12}ON_2S_2$ requires C, 50·0; H, 5·0; N, 11·7; S, 26·7%). This ester was hydrolysed to 1-aminobenzthiazole as in the case of the lower homologue.

By heating 1-thiocyanobenzthiazole on the steam-bath with the appropriate alcohols, the following esters of benzthiazyl-1-thioncarbamic acid were prepared: *n*-butyl, m. p. 105°; *iso*propyl, m. p. 174°; *cyclo*hexyl, m. p. 146°; amyl, m. p. 116°; and β-ethoxyethyl, m. p. 125°.

(ix) *With methyl-alcoholic hydrogen chloride.* 1-Thiocyanobenzthiazole (3·8 g.) was added to methyl alcohol (50 c.c.) at 0°; with good stirring, the suspension was saturated with hydrogen chloride at 0°. After several days, the solution was filtered, poured into water, and basified. The neutral material, isolated by extraction with ether, was 1-methylthiobenzthiazole (2·23 g., 61%), m. p. and mixed m. p. with authentic material 43—47°. Only traces of acid-soluble and alkali-soluble products were obtained.

The authors thank I.C.I. (Dyestuffs) Ltd. for permission to publish these results.

RESEARCH DEPARTMENT, I.C.I. (DYESTUFFS), LTD., BLACKLEY, MANCHESTER, 9.

[*Received, August 9th*, 1943.]

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## 7. *The Synthesis of Amino-acids from Substituted Cyanoacetic Esters.*

By PAUL E. GAGNON, ROGER GAUDRY, and F. E. KING.

The synthesis of amino-acids from substituted cyanoacetic esters by the Curtius reaction (Darapsky, *J. pr. Chem.*, 1936, **146**, 250) has been successfully applied to the preparation of valine, phenylalanine, and tyrosine.

$$\underset{\text{(I.)}}{R{\cdot}CH(CN){\cdot}CO_2Et} \longrightarrow \underset{\text{(II.)}}{R{\cdot}CH(CN){\cdot}NH{\cdot}CO_2Et} \longrightarrow \underset{\text{(III.)}}{R{\cdot}CH(CO_2H){\cdot}NH_2}$$

The failure of experiments to extend the method, for example, to the synthesis of the diamino-acids ornithine and lysine from ethyl α-cyanoadipate and ethyl α-cyanopimelate, indicates that it is not of wide application.

IT has been shown that amino-acids may be obtained by applying the Curtius reaction to the monohydrazides of the dicarboxylic acids (Curtius, *J. pr. Chem.*, 1930, **125**, 211), but the preparation of these acid hydrazides is laborious and constitutes a disadvantage of the method. For the synthesis of α-amino-acids, Darapsky (*ibid.*, 1936, **146**, 250) has employed the more accessible alkylcyanoacetic esters (I), which readily afford monohydrazides. These undergo degradation in the usual manner, hydrolysis at the urethane stage (II) also affecting the cyano-group and thus giving the amino-acid (III).

Although apparently of general application, the synthesis has been used to prepare only three amino-acids, namely, leucine, α-amino-*n*-valeric acid, and α-amino-δ-methylhexoic acid (Darapsky, *loc. cit.*). The following experiments were undertaken in order to extend it to amino-acids of other types.

Experience of the reaction was gained by the synthesis of valine (III, R = $CHMe_2$). For this, α-cyano-β-methylbutyrhydrazide was converted by nitrous acid into the azide and thence into the ethyl urethane by heating with alcohol. Hydrolysis with boiling hydrochloric acid afforded *dl*-valine, characterised by the *phenylcarbamyl* derivative, $Ph{\cdot}NH{\cdot}CO{\cdot}NH{\cdot}CH(CO_2H){\cdot}CHMe_2$, which was obtained by reaction with phenyl *iso*cyanate and alkali.

By the same sequence of reactions phenylalanine (III, R = $CH_2Ph$) was conveniently obtained from *α-cyano-β-phenylpropionhydrazide*, and the amino-acid was analysed in the form of its *phenylcarbamyl* derivative. Similarly, the *hydrazide* of α-cyano-β-anisylpropionic acid gave *dl*-tyrosine when the cyanourethane was hydrolysed by mixed concentrated hydrochloric and acetic acids; with diluted acid, *O*-methyltyrosine was the product.

For attempting the synthesis of ornithine, γ-phenoxypropyl bromide was condensed with ethyl cyanoacetate, and the *hydrazide* of the resulting α-cyano-δ-phenoxyvaleric acid degraded by the standard procedure.

The final hydrolysis with hydrochloric acid gave *α-amino-δ-phenoxyvaleric acid* (III, R = PhO·$CH_2$·$CH_2$·$CH_2$): more drastic reagents, *e.g.*, hydrobromic acid, destroyed the cyanourethane.

The possibility that cyanodicarboxylic acids might yield diamino-acids by the Curtius reaction was investigated with the *dihydrazides* prepared from ethyl cyanoadipate and from its homologue ethyl cyanopimelate. From both, diurethanes appeared to be formed in the usual way, but these were destroyed by the hydrolytic agent.

Ethyl αβ-dicyanopropionate, the appropriate ester for the synthesis of aspartic acid, gave only resinous products with hydrazine, and it therefore seems unlikely that the Darapsky method can afford amino-dicarboxylic acids.

## Experimental.

dl-*Valine*.—Hydrazine hydrate (24 g. of 100%) reacted exothermally with ethyl *iso*propylcyanoacetate (Fischer, *Ber.*, 1909, **42**, 2983) (92 g.) to give a pale yellow syrup. This was set aside in an evacuated desiccator to remove alcohol, but could not be crystallised. A solution of the crude hydrazide (46 g.) in hydrochloric acid (400 c.c. of 25%) was cooled to 0° and stirred under a layer of ether (200 c.c.) while sodium nitrite (34 g.), dissolved in water (50 c.c.), was added. The dried ethereal layer was then mixed with absolute alcohol (300 c.c.) and heated on a water-bath under a short fractionating column until the ether had distilled. After boiling for 1 hour to complete the evolution of nitrogen, alcohol was removed under reduced pressure, and the syrupy product heated under reflux with hydrochloric acid (300 c.c. of 20%) in an oil-bath for 48 hours. The straw-coloured solution was then evaporated under diminished pressure, and the residue taken up in water and neutralised with ammonia. The addition of an equal volume of alcohol precipitated *dl*-valine, which was collected on the next day and recrystallised from water (22—23 g.; 60% yield). A crystalline derivative was prepared by dissolving the amino-acid in an equivalent of aqueous sodium hydroxide and shaking with the calculated amount of phenyl *iso*cyanate. The filtered solution was acidified, and this precipitated dl-α-N-*phenylcarbamido*isovaleric acid, which formed colourless thin leaflets, m. p. 149°, after crystallisation from aqueous alcohol (Found: N, 12·0. $C_{12}H_{16}O_3N_2$ requires N, 11·9%).

*Ethyl α-Cyano-β-phenylpropionate* (cf. Hessler, *Amer. Chem. J.* 1899, **22**, 169: Walker, J., 1924, **125**, 1622).—Ethyl cyanoacetate (65 g.; 2 mols.) and benzyl bromide (50 g.) were dissolved in a solution of sodium (6·7 g.) in absolute alcohol (125 c.c.), which was refluxed on a steam-bath for 2 hours. After removal of the alcohol the product was shaken with water and ether, and the dried ethereal extract evaporated and fractionated. The portion, b. p. 160—188°/15 mm., was redistilled, and the α-cyano-β-phenylpropionic ester, b. p. 165—173°/15 mm. (26 g.; 44% yield), mixed with hydrazine hydrate (6·5 g. of 100%). After some minutes a vigorous reaction set in, and when cool the product solidified. Recrystallisation from alcohol gave the *hydrazide* (21 g.) in shining plates, m. p. 123—124° (Found: C, 63·7; H, 5·8. $C_{10}H_{11}ON_3$ requires C, 63·5; H, 5·8%). From the ester fractionation, ethyl α-cyano-ββ-dibenzylacetate (10 g.), b. p. 190—200°/15 mm., was isolated; it was identified by means of the *hydrazide*, m. p. 235—237°, which crystallised from alcohol in microscopic prisms (Found: C, 72·9; H, 6·0. $C_{17}H_{17}ON_3$ requires C, 73·1; H, 6·1%).

dl-*Phenylalanine*.—α-Cyano-β-phenylpropionhydrazide (10 g.), in ice-cold water (50 c.c.) and concentrated hydrochloric acid (75 c.c.) covered by ether (100 c.c.), was converted into the azide by addition of sodium nitrite (8 g.) in a little water. The dried ethereal solution of the product was added to alcohol (100 c.c.), which was heated to expel the ether, then refluxed for an hour, and finally evaporated. The residue (11 g.) was hydrolysed by refluxing (oil-bath) for 48 hours with hydrochloric acid (200 c.c. of 20%), and the material obtained by evaporation of the filtered liquid (charcoal) under reduced pressure was dissolved in water (10 c.c.). The solution was brought to the isoelectric point (pH = 5·9) with aqueous ammonia, and after an equal volume of alcohol had been added, phenylalanine (4 g., 50% yield) separated, m. p. 265° when crystallised from water. The *phenylcarbamyl* derivative, prepared from an alkaline solution of the amino-acid and phenyl *iso*cyanate, separated from aqueous alcohol as a white powder, m. p. 168—170° (Found: C, 67·9; H, 5·6. $C_{16}H_{16}O_3N_2$ requires C, 67·6; H, 5·6%).

*Ethyl α-Cyano-β-anisylpropionate*.—Ethyl cyanoacetate (80 g.; 2 mols.) and anisyl chloride (55 g.) were dissolved in a solution of sodium (8·1 g.) in alcohol (150 c.c.) heated for 3 hours under reflux on a steam-bath, and the oil obtained by pouring into water was collected in ether and distilled. The fraction (39 g.; 48% yield), b. p. 165—170°/0·2 mm., was treated with hydrazine hydrate (1 mol. of 100%), and after leaving overnight the solid *hydrazide* (36 g.) was obtained, m. p. 122—123° when crystallised from alcohol (Found: N, 19·5. $C_{11}H_{13}O_2N_3$ requires N, 19·2%).

dl-*Tyrosine*.—α-Cyano-β-anisylpropionhydrazide (36 g.) reacted with nitrous acid under the conditions given for the preparation of phenylalanine, except that the formation of the hydrazide was slower. When the viscous urethane obtained by boiling with alcohol was refluxed for 40 hours with 20% hydrochloric acid and the solution neutralised, the sparingly soluble *dl-O*-methyltyrosine (yield, 30%) was obtained (negative Millon test).

Refluxing the urethane (36 g.) with concentrated hydrochloric acid (300 c.c.) and glacial acetic acid (300 c.c.) gave a dark solution, which was then evaporated. The residue was shaken with water, and the insoluble matter removed, addition of ammonia to the charcoaled solution precipitating *dl*-tyrosine in characteristic woolly needles at pH 5·7 (Found after five crystallisations and drying under reduced pressure over phosphoric oxide: C, 59·5; H, 6·6. Calc. for $C_9H_{11}O_3N$: C, 59·6; H, 6·1%) (yield, 3·3 g.; 11%).

*Ethyl α-Cyano-δ-phenoxyvalerate*.—Ethyl cyanoacetate (57 g.) and γ-phenoxypropyl bromide (108 g.) were heated in a solution of sodium (11·5 g.) in alcohol (300 c.c.) under reflux on a steam-bath for 1 hour. The crude cyanophenoxyvalerate (50 g.; 40%), b. p. 175—190°/0·7 mm., was isolated by fractionating the oily product obtained on pouring into water. A mixture with hydrazine hydrate (1 mol. of 100%) solidified on cooling, and by crystallisation from alcohol the *hydrazide* of α-cyano-δ-phenoxyvaleric acid formed colourless minute needles, m. p. 85°, turning pink in air (Found: C, 61·7; H, 6·4. $C_{12}H_{15}O_2N_3$ requires C, 61·8; H, 6·4%).

*α-Amino-δ-phenoxyvaleric Acid*.—Conversion of the hydrazide of α-cyano-δ-phenoxyvaleric acid into the syrupy urethane followed the general procedure. The product (20 g.) was refluxed with hydrochloric acid (200 c.c. of 20%), and the filtered solution (charcoal) evaporated. The residue was dissolved in water (10 c.c.) and neutralised with ammonia, whereupon dl-*α-amino-δ-phenoxyvaleric acid* (7 g.; 40% yield) was precipitated. It was recrystallised from boiling water, and separated as a white powder, m. p. 265—267° (decomp.) (Found: C, 63·2; H, 7·1. $C_{11}H_{15}O_3N$ requires C, 63·1; H, 7·2%). The action of phenyl *iso*cyanate on a concentrated alkaline solution of the acid gave a *phenylureide*, which separated from aqueous alcohol as a micro-crystalline powder, m. p. 158° (Found: N, 8·5. $C_{18}H_{20}O_4N_2$ requires N, 8·5%).

*Ethyl α-Cyanoadipate*.—The condensation of ethyl γ-bromobutyrate (40 g.) and ethyl cyanoacetate (25 g.) in a solution of sodium (4·8 g.) in alcohol (100 c.c.) refluxing on a steam-bath for 2 hours gave, on pouring into water, an oil, from which the fraction (19 g.; 40% yield), b. p. 178—186°/15 mm., was isolated. It formed with hydrazine hydrate a syrup which eventually solidified and was crystallised, though with appreciable loss, from alcohol. The pure *cyanoadipodi-*

*hydrazide*, m. p. 128°, was very soluble in water (Found : N, 34·9. $C_7H_{12}O_2N_8$ requires N, 35·2%). It was submitted to the sequence of operations necessary to produce the corresponding diurethane, but when the viscous product was heated (oil-bath) under reflux for 48 hours with hydrochloric acid (20%), only amorphous material was obtained from which no crystalline derivatives (dibenzoate, dipicrate) could be prepared.

*Ethyl α-Cyanopimelate.*—A mixture of ethyl δ-bromovalerate (35 g.) with ethyl cyanoacetate (37 g.; 2 mols.), heated in a solution of sodium (3·9 g.) in alcohol (100 c.c.) at 100° for 3 hours, gave, after the appropriate treatment, a colourless oil (21 g.; 30% yield), b.p. 183—197°/12 mm., from which was prepared *cyanopimelodihydrazide*. It separated slowly from a fairly large volume of alcohol as a white powder, m. p. 115—116° (Found : N, 33·0. $C_8H_{16}O_2N_8$ requires N, 32·9%). As with its lower homologue, degradation *via* azide and urethane yielded only resinous material.

Ethyl *αβ*-dicyanopropionate (Thorpe, J., 1906, **89**, 1461) reacted violently with hydrazine hydrate (50%), giving a brown resin, soluble in dilute mineral acid but insoluble in organic solvents. A similar product slowly formed when the reaction was conducted at 0° in alcoholic solution, which was afterwards evaporated in an evacuated desiccator. The ester and aqueous hydrazine (6%) were therefore cautiously mixed and cooled, and the solution then acidified and treated with nitrite under ether in the usual way. A dark flaky solid separated insoluble in ether and not showing any properties of an azide.

The authors thank the Rhodes Trustees for a Scholarship awarded to one of them (R. G.).

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[*Received, August 25th*, 1943.]

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## 8. *Decomposition of the Diazonium Salts of 4-Nitro-1-naphthylamine by Sodium Sulphite and Sodium Acetate. Preparation of 4 : 4′-Dinitro-1 : 1′-azonaphthalene.*

By HERBERT H. HODGSON, DONALD E. NICHOLSON, and GERALD TURNER.

4-Nitronaphthalene-1-diazonium chloride or sulphate is decomposed by sodium sulphite to give mainly 4 : 4′-*dinitro*-1 : 1′-*azonaphthalene* (10—20%) and 4 : 4′-dinitro-1 : 1′-dinaphthyl (*ca.* 50%). Sodium acetate alone initiates an oxidation–reduction reaction from which the above products result, and also a simultaneous decomposition by water or hydroxyl ions to give eventually 4 : 4′-*dinitronaphthalene*-1′ : 2-*azo*-1-*naphthol*. If excess of sodium acetate is added before the sodium sulphite, the product is almost entirely 4 : 4′-dinitro-1 : 1′-azonaphthalene.

SULPHITES in neutral or alkaline solution act on diazo-compounds to give diazosulphonates, $Ar{\cdot}N{:}N{\cdot}SO_3M$, where M is an atom of a univalent metal or its equivalent. This reaction, one of the most general and reliable of those of the diazo-compounds, rarely fails, and crystalline, stable, and easily isolated salts are nearly always obtained. Naphthalene-α- and -β-diazonium salts are among the few exceptions, αα′- (Lange, D.R.-P. 78,225; Friedländer, Vol. 4, 1016) and ββ′-azonaphthalene (Hantzsch and Schmiedel, *Ber.*, 1897, **30**, 80) being formed respectively when these substances are treated with sodium sulphite.

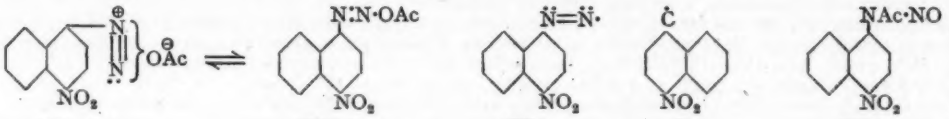
It appeared of interest, therefore, to ascertain whether the sulphonates of substituted diazonaphthalenes would react like the parent compounds, and also to elucidate the mechanism of the reaction in the naphthalene series. The procedure adopted was similar to that of Lange; 4-nitro-1-naphthylamine was diazotised either in hydrochloric acid or by Hodgson and Walker's method (J., 1933, 1620), sodium acetate added in excess of the amount required to react with all the mineral acid, and the requisite amount of an aqueous solution of sodium sulphite then stirred rapidly into the mixture. Reaction commenced immediately, with brisk evolution of nitrogen and precipitation of a mixture of 4 : 4′-*dinitro*-1 : 1′-*azonaphthalene* and sodium 4-nitronaphthalene-1-diazosulphonate; the latter disappeared after several hours, with formation of the former. Only a small amount of 4-nitro-1-naphthol was produced by a side reaction, and in so far as the sulphonate was decomposed, the reaction was nearly quantitative. No azo-dye was formed (compare below), and no α-nitronaphthalene could be detected when either the precipitate or the filtrate therefrom was steam-distilled, the filtrate, however, affording a little more 4 : 4′-dinitro-1 : 1′-azonaphthalene.

When only sodium acetate was allowed to react with the above diazonium solution, the colour rapidly changed to deep yellow, and after a few minutes formation of a red precipitate occurred and continued for several hours until decomposition of diazoacetate was almost complete. This precipitate consisted mainly of 4 : 4′-dinitro-1 : 1′-dinaphthyl, 4 : 4′-dinitro-1 : 1′-azonaphthalene (I), and 4 : 4′-*dinitronaphthalene*-1′ : 2-*azo*-1-*naphthol* (II), a small amount of naphthalene-1 : 4-diazo-oxide and unidentified oxidation products.

Finally, if sodium sulphite reacts alone with the mineral acid solution of the diazonium compound, there is violent evolution of sulphur dioxide and nitrogen, and formation of numerous products, including 4 : 4′-dinitro-1 : 1′-azonaphthalene (10—20%), 4 : 4′-dinitro-1 : 1′-dinaphthyl, α-nitronaphthalene, sodium 4-nitronaphthalene-1-diazosulphonate, and unidentified substances. No azo-dye (II) was produced.

From these experiments it follows that, although 4 : 4′-dinitro-1 : 1′-azonaphthalene is formed whatever the variations, yet a good yield is obtained only when addition of excess of sodium acetate precedes that of sodium sulphite. The mechanism of the latter reaction would appear to be initial formation of an equilibrium mixture of 4-nitronaphthalene-1-diazonium acetate (III*a*) and 4-nitronaphthalene-1-diazoacetate (III*b*), followed by reduction of (III*a*) by electron acceptance from the sodium sulphite to the radicals (IV) and (V), which then unite to form the azo-compound (I). The equilibrium mixture, (III*a*) $\rightleftharpoons$ (III*b*), would then continue to replace (III*a*) until all had reacted. The presence of a very small amount of 4-nitro-1-naphthol would appear to be due to the usual decomposition of diazonium salts by aqueous acids, and the absence of

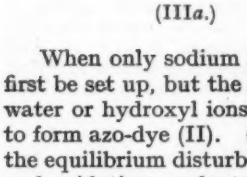
azo-dye (II) would be explained by the slow rate of coupling of the diazo-acetate (III*b*) compared with its rapid rearrangement to (III*a*) and subsequent decomposition as above.



(III*a*.) (III*b*.) (IV.) (V.) (VI.)

When only sodium acetate is added to the diazonium salt solution, the equilibrium (III*a*) ⇌ (III*b*) will first be set up, but the following simultaneous reactions then occur: (1) Decomposition of (III*a*) by anionoid water or hydroxyl ions in the normal manner to form 4-nitro-1-naphthol, which will then couple with (III*b*) to form azo-dye (II). (2) Decomposition of (III*a*) by an oxidation–reduction process, doubtless facilitated by the equilibrium disturbance necessitated by reaction (1), whereby radicals (IV) and (V) result on the one hand, and oxidation products on the other. Combination of (IV) and (V) will afford (I), whereas union of two (IV) affords 4 : 4′-dinitrodinaphthyl. The latter reaction is closely allied to those reported by Hodgson and Marsden (J., 1940, 208), and by Elks, Haworth, and Hey (J., 1940, 1284) for the preparation of biaryl compounds. The oxidation products were all soluble in acetone. After being kept overnight, the sodium acetate mixture still contained undecomposed diazo-compound, although coupling with alkaline β-naphthol was very slow and might well indicate the presence of the *anti*-form of (III*b*), or even the nitrosoamine form (VI). Hydrochloric acid, however, at once converts the slow-coupling compound into 4-nitronaphthalene-1-diazonium chloride.

The most complex case is when sodium sulphite is added alone to the mineral acid solution of the diazonium salt, since there is now present free sulphur dioxide, which could not be detected when the solution had been previously saturated with sodium acetate. About 25% of the product, extracted by boiling alcohol, melted below 200°, but could not be purified. Also, after several days the mixture still contained undecomposed sulphonate, which could be reoxidised to 4-nitronaphthalene-1-diazonium salt, and subsequently coupled with alkaline β-naphthol to give 4′-nitronaphthalene-1′ : 1-azo-2-naphthol (VII).



(VIII.)

4 : 4′-Dinitro-1 : 1′-azonaphthalene gives a bright pure blue colour with concentrated sulphuric acid, which suggests that salt formation has produced a diindamine-like structure (VIII). Dilution with water changes the blue to a bright yellow, and these colours afford a characteristic qualitative test for the presence of the azo-compound. The great stability of (I) was also shown by a marked tendency to sublime when heated.

In all the reactions described the formation of 4 : 4′-*dinitronaphthalene*-1′ : 2-*azo*-1-*naphthylamine* (IX), though expected, was never observed.

## Experimental.

*Action of Sodium Sulphite on 4-Nitronaphthalene-1-diazonium Chloride (or Sulphate).*—4-Nitro-1-naphthylamine (4·7 g.) was ground with hydrochloric acid (10 c.c., *d* 1·16) and water (15 c.c.), ice (5 g.) added, and a solution of sodium nitrite (2 g.) in water (10 c.c.) stirred into the mixture as rapidly as possible. Most of the paste passed into solution, and after a further addition of water (10 c.c.), the liquid was filtered and treated at 0° with hydrated sodium sulphite (4 g.) in water (20 c.c.). Sulphur dioxide and nitrogen were evolved, and after being kept cold overnight, the red-brown solid (4—5 g.) was collected and washed with cold water until the washings were only pale yellow. The filtrate did not couple with alkaline β-naphthol, but did so after cautious treatment with bromine water, or with potassium chromate preceded by neutralisation, to give 0·3 g. of 4′-nitronaphthalene-1′ : 1-azo-2-naphthol (VII), thereby showing the presence of unchanged sulphonate; when excess of bromine water is used, 4-nitronaphthalene-1-diazoperbromide is precipitated. If the initial reaction mixture was kept for 3 days before the filtrate was oxidised and coupled with alkaline β-naphthol, the weight of (VII) decreased to 0·2 g., indicating a very gradual decomposition of the diazosulphonate. Steam distillation of the red-brown solid removed α-nitronaphthalene (0·12 g., *i.e.*, 2—3%), and the flask liquor still contained diazosulphonate, as established by its oxidation with bromine water and hydrochloric acid to 4-nitronaphthalene-1-diazonium chloride.

After steam distillation, the red-brown solid had m. p. 145—150°; extraction by ethyl alcohol (Soxhlet) removed 25% of it, and the residue then had m. p. 229°; the extract on cooling deposited a microcrystalline mixture, m. p. 140—152° (Found: N, 11·4%), but no constituent could be identified. Boiling 8% aqueous sodium hydroxide also extracted about 25%. The residue from the alcoholic extraction was extracted by acetone (Soxhlet), a further 50% being removed, and the m. p. of the residue rising to 318—320°. This 4 : 4′-*dinitro*-1 : 1′-*azonaphthalene* crystallised from boiling nitrobenzene in short red needles, m. p. 334° (Found: N, 15·3. $C_{20}H_{12}O_4N_4$ requires N, 15·1%), almost insoluble in boiling alcohol, slightly soluble in boiling glacial acetic acid to give a yellow solution, and sparingly soluble in acetone and boiling benzene or chlorobenzene; its colour reactions are described above and in the table. When carefully heated to the m. p., preferably in a vacuum, this azo-compound gave a sublimate of orange needles, m. p. 334°; and alcoholic potassium hydroxide apparently reduced it very readily to a chocolate-brown powder which no longer gave a blue colour with concentrated sulphuric acid, indicating that the nitro-groups had been attacked.

The acetone extract (above), when concentrated, deposited micro-crystals of impure 4 : 4′-dinitro-1 : 1′-dinaphthyl, m. p. 230—240°, raised by several recrystallisations from acetone and benzene to 246° (Found: N, 8·3. Calc.: N, 8·1%). The fraction removed by acetone, when refluxed with boiling glacial acetic acid containing a little concentrated hydrochloric acid and treated with zinc dust in small quantities until a clear solution was obtained, afforded a small amount of 4 : 4′-di(acetamido)-1 : 1′-dinaphthyl, which crystallised from the hot filtered solution on cooling; m. p. 364° (Cumming and Howie, J., 1932, 530, give m. p. 363—364°) (Found: N, 7·8. Calc.: N, 7·6%). No colour reactions (see table) were obtained for (II).

*Colour Reactions of the Azo-compounds described.*

| Compound. | Conc. $H_2SO_4$. | $COMe_2$, followed by NaOH. | Alcoholic KOH. |
|---|---|---|---|
| (I), m. p. 334° | Pure blue, with yellow halo on standing. Dilution with water changes blue to bright yellow | Very sparingly soluble in acetone. No colour when NaOH added | Insoluble but rapidly reduced, especially on heating, to a chocolate-brown powder |
| (II), m. p. 278° | Initial blue-violet, changing to red-violet which persists on addition of water | Red, changing to blue-violet with NaOH | Permanganate-violet solution, unchanged on gentle heating |
| (VII), m. p. 258° | Purple, but bluer than (II). Vanishes on addition of water | Scarlet, changing to reddish-blue. Red on dilution | Violet |
| (IX), m. p. 274° | Initial blue, changing to red-violet and purple. Colour vanishes on addition of water | Scarlet solution, changing to blue-green with NaOH, and to green on standing | Blue-violet, changing to blue and then to deep green on heating |

*Action of Sodium Acetate on 4-Nitronaphthalene-1-diazonium Chloride (or Sulphate).*—A solution of the diazonium chloride, obtained as above from 4-nitro-1-naphthylamine (4·7 g.), was mixed rapidly with a solution of sodium acetate in amount sufficient to provide 50% excess over the hydrochloric acid. The deep yellow solution produced began to redden rapidly after a few minutes and then to deposit a dull maroon-brown precipitate, m. p. 250—256° (Found : N, 9·2%), which crystallised from nitrobenzene in a mixture of micro-crystals, m. p. 288—290° (with red sublimate of m. p. 280°). This mixture gave colour reactions for both (I) and (II); and although several recrystallisations from nitrobenzene failed to effect a clear separation, nevertheless the m. p. was raised to 316°. When the mixture was heated in the vacuum sublimator, (I) was obtained pure in small quantity as an orange sublimate, m. p. 334° (Found : N, 15·3%), but the red sublimate of (II) was admixed with (I). Of the initial precipitate above, boiling alcohol extracted only *ca.* 5—10%, and this extract on cooling deposited micro-crystals of 4 : 4′-dinitro-1 : 1′-dinaphthyl, which, when recrystallised several times from benzene or glacial acetic acid, had m. p. 246° (Found : N, 8·3. Calc. : N, 8·1%). Subsequent extraction with acetone (Soxhlet) removed *ca.* 50% more of the mixture, the final residue (40%) having m. p. 292° (Found : N, 14·1%). The acetone extract on concentration deposited 4 : 4′-dinitro-1 : 1′-dinaphthyl, m. p. 200—240°, raised to 246° after several recrystallisations from acetone and benzene (Found : N, 8·2%), but the compounds still dissolved in the acetone could not be resolved and were probably the oxidation products of the original oxidation–reduction process.

When either the initial product or the residue after acetone extraction was shaken vigorously for a few seconds with alcoholic potassium hydroxide, and the liquid rapidly filtered and rendered acid, 4 : 4′-*dinitronaphthalene-1′* : 2-*azo*-1-*naphthol* (II) was precipitated; after two crystallisations from nitrobenzene it was obtained in short, red parallelepipeds, m. p. 278° (Found : N, 14·5. $C_{20}H_{12}O_5N_4$ requires N, 14·4%). The undissolved part containing the 4 : 4′-dinitro-1 : 1′-azonaphthalene was attacked by the alcoholic potash and no longer gave the colour reactions of (I). When the reaction product with sodium acetate was treated in the cold with 20 times its weight of fuming nitric acid (*d*, 1·5), kept for 20 minutes, and then poured on ice, the precipitate contained 2 : 4-dinitro-1-naphthol and the filtrate from it coupled with alkaline β-naphthol to give (VII).

This reaction with sodium acetate started fairly rapidly but soon became slow, and a solution of the diazonium chloride was always obtained on acidification with hydrochloric acid after precipitation had practically ceased. Only a small amount of naphthalene-1 : 4-diazo-oxide was formed, which, when dissolved in a mixture of glacial acetic and sulphuric acids, was deaminated to α-naphthol by alcoholic cuprous oxide (Hodgson and H. S. Turner, J., 1942, 748).

*Action of Sodium Sulphite on 4-Nitronaphthalene-1-diazoacetate* (in part with J. Habeshaw).—4-Nitro-1-naphthylamine (18·8 g.) was diazotised as above, and also by the method of Hodgson and Walker (*loc. cit.*) : the amine was dissolved in glacial acetic acid (188 c.c.), the solution added below 20° to sulphuric acid (60 c.c., *d* 1·84) in which sodium nitrite (7 g.) had been dissolved, and ice (600 g.) added. Both diazo-solutions were rapidly treated with an aqueous solution of sodium acetate in 50% excess over that required to react with all the mineral acid, and then as quickly as possible mixed with a solution of neutral sodium sulphite (10 g.) in water (500 c.c.) containing ice. (Speed is essential in order to obviate the reactions caused by sodium acetate alone.) Nitrogen was evolved but no sulphur dioxide, and a solid separated, the light orange colour of which deepened on keeping. If filtered off too soon and dried, the precipitate exploded on heating, showing the presence of diazosulphonate, but after being kept overnight, when filtered off and dried (15·9 g.), it had m. p. 305—312°. The deep red filtrate contained a little 4-nitro-1-naphthol, and on heating deposited a small amount of 4 : 4′-dinitro-1 : 1′-azonaphthalene. No α-nitronaphthalene could be obtained by steam distillation of either filtrate or precipitate, but a little 4-nitro-1-naphthol was extracted from the latter by 10% aqueous sodium hydroxide; the residue of almost pure 4 : 4′-dinitro-1 : 1′-azonaphthalene then crystallised from nitrobenzene in red needles, m. p. 334° (Found : N, 15·3%); reductive acetylation (see Hodgson and Nicholson, J., 1940, 206) gave 1 : 4-diacetylnaphthylenediamine in colourless crystals, m. p. 304° (Kleeman, *Ber.*, 1886, **19**, 334, gives m. p. 303—304°) (Found : N, 11·7. Calc. : N, 11·6%). The colour reactions for (II) were not observed.

*Preparation of* 4 : 4′-*Dinitronaphthalene-1′* : 2-*azo*-1-*naphthol* (II).—4-Nitro-1-naphthylamine (1·8 g.) was diazotised as described above, and the filtered solution stirred at 0° into one of 4-nitro-1-naphthol (2 g.) in water (100 c.c.) containing sodium hydrogen carbonate (5 g.). Immediate precipitation of the dye occurred, and after 30 minutes it was filtered off, washed, dried, and recrystallised from nitrobenzene, separating in copper-coloured needles, m. p. 278° (Found : N, 14·4%). When sodium hydroxide was used instead of the bicarbonate, only partial precipitation occurred, but on cautious neutralisation of the alkaline filtrate with acetic acid the remainder of the dye was obtained : the stronger alkali had probably converted part of the 4-nitronaphthalene-1-diazonium chloride into the sodium salt of the less reactive (*anti*-) form of 4-nitronaphthalene-1-diazotate.

*Preparation of* 4 : 4′-*Dinitronaphthalene-1′* : 2-*azo*-1-*naphthylamine* (IX).—4-Nitro-1-naphthylamine was diazotised in hydrochloric acid as above, the excess of nitrous acid destroyed by urea, and the solution stirred into an equivalent amount of a fine suspension of 4-nitro-1-naphthylamine (made from a chilled solution in hot glacial acetic acid) to which an excess of sodium acetate over all the hydrochloric acid had been added. A slow reaction occurred, as indicated by the yellow suspension becoming red. After being kept overnight, the solid was filtered off and dissolved in boiling nitrobenzene, from which it separated in chocolate-brown prisms, m. p. 274°, depressed by admixture with the naphthol (II) (Found : N, 18·3. $C_{20}H_{13}O_4N_5$ requires N, 18·1%); it was sparingly soluble in acetone, giving a scarlet solution.

The authors thank I.C.I. (Dyestuffs) Ltd. for various gifts.

Technical College, Huddersfield. [*Received, August 5th*, 1943.]

# 9. An Interpretation of the Sandmeyer Reaction. Part IV. Catalysed Decomposition of Diazonium Kations by Anionoid Complexes with Special Reference to those of Cobalt and Ferric Iron.

By Herbert H. Hodgson, Stanley Birtwell, and John Walker.

The catalysed decompositions described in Part III (J., 1942, 720) have now been conducted for both diazotised *m*- and *p*-nitroaniline in hydrochloric acid solution of *d* 1·16. At this acid concentration, ferric chloride and cupric chloride are practically as efficient as cuprous chloride. Cobalt chloride in the blue complex anionoid condition appreciably catalyses the reaction, whereas in the pink kationoid state it has lost its catalytic influence. These experiments provide additional evidence for the anionoid mechanism suggested in Part I (J., 1941, 770).

In Part III (*loc. cit.*) replacement of the diazonium group in *p*-nitrobenzenediazonium chloride by chlorine was effected by anionoid complexes in two concentrations of hydrochloric acid, and the alteration in water content affected the yields of *p*-chloronitrobenzene. Since increase in hydrogen chloride concentration resulted in increased replacement by chlorine, it follows that this must be ascribed to the increase in concentration of the anionoid complex in the stronger acid, the simultaneous reaction by anionoid water with production of *p*-nitrophenol showing a corresponding decrease. It appeared of interest, therefore, to carry out the reactions in concentrated hydrochloric acid (*d* 1·16), for which purpose solutions of *m*- and *p*-nitroaniline were diazotised by addition of solid sodium nitrite, and the resulting diazonium salt solutions decomposed, while just boiling, by the addition of metallic chlorides whose metals are prone to form complex halogeno-anions, *viz.*, those of aluminium, antimony chromium, cobalt, copper (cuprous and cupric), iron (ferric), mercury(ic), nickel, tin (stannic), zinc. On addition of the sodium nitrite, sodium chloride was precipitated, so that all the solutions were saturated thereby, and all the decompositions were thus carried out under practically the same conditions, except for the small differences in boiling points of the various solutions. Under the more concentrated conditions, the yield of *p*-chloronitrobenzene by hydrochloric acid alone became 54·4% against 41% under the more dilute conditions of Part III (*loc. cit.*, Table III), indicating that it is the chlorine of the un-ionised hydrogen chloride which is the active agent in the replacement and not the chlorine ion (cf. Part I, J., 1941, 770). This result is in substantial agreement with the earlier views of Hantzsch (*Ber.*, 1900, **33**, 2534) and the deductions of Waters (J., 1939, 868) on the activity of un-ionised hydrogen chloride in the decomposition of benzenediazonium chloride in very concentrated aqueous solution, or in concentrated hydrochloric acid, where the yield of chlorobenzene falls off very rapidly as the solution is diluted.

A noteworthy feature of the decompositions of diazotised *p*-nitroaniline is the efficiency of ferric and cupric chlorides as catalysts, a 77·6% yield of *p*-chloronitrobenzene (previously 63%) being obtained, *i.e.*, the same as that with cuprous chloride under like conditions. On the other hand, aluminium chloride only slightly increased the yield over the blank, and calcium, chromium, mercuric, and zinc chlorides had no effect upon it. In marked contrast, antimony trichloride reduced the yield to 37·1% (blank, 54·4%), a similar effect having already been observed under more dilute conditions (41% to 32%), and it would appear that antimony chloride activates anionoid water preferentially to chlorine.

The experiments with cobalt chloride have an interesting bearing on its ionic state. When anhydrous, or in solutions of high chloride-ion concentration, it is blue, owing, it is generally supposed, to the $[CoCl_4]^{--}$ anion, and such solutions afford a 70·9% yield of chloro-compound, whereas the more aqueous pink solution, containing $Co(H_2O)_6Cl_2$, gives a yield of only about 10%, *i.e.*, the same as that in hydrochloric acid at the same dilution with no cobalt present. Also, when *p*-nitroaniline is diazotised by Hodgson and Walker's method (J., 1933, 1620) in concentrated sulphuric–glacial acetic acid solution, and then decomposed by the blue solution of cobalt chloride in concentrated hydrochloric acid, the yield is decreased to that of the blank (40·5%), showing that the dissociation of the complex ion in the composite solution had inhibited its efficiency for replacement of the diazonium group by chlorine. These experiments with cobalt chloride support the interpretation given for the previous results with cupric chloride, and with copper sulphate and sodium bromide (Part III), that the decomposition is due to the complex $[CuCl_4]^{---}$ or $[CuBr_4]^{---}$ anion. In this connection, it is of interest that anhydrous cupric bromide is black, this colour being ascribed to $Cu[CuBr_4]$, and that the addition of sodium bromide to copper sulphate in the experiments referred to in Part III (*loc. cit.*) produced a colour change from blue to green-brown, due probably to the formation of the $[CuBr_4]^{--}$ anion; in like manner, cupric chloride is held to be $Cu[CuCl_4]$ (cf. Emeléus and Anderson, "Modern Aspects of Inorganic Chemistry," 1938, p. 144).

The great efficiency of ferric chloride in concentrated hydrochloric acid solution must also be ascribed to the formation of a complex anion, and there is considerable evidence for the existence of $HFeCl_4$ (cf. Mellor, "A Comprehensive Treatise on Inorganic and Theoretical Chemistry," Vol. XIV, p. 75).

The experiments with *m*-nitroaniline usually gave somewhat lower yields of *m*-chloronitrobenzene, but in every case in the same order of efficiency as those with *p*-nitroaniline (see table). In these reactions also, ferric and curpric chlorides proved to be as efficient as cuprous chloride, and the decreased yields were to be anticipated in view of the lower positivity of the significant carbon atom to which the diazonium group is attached (cf. Part I, *loc. cit.*).

## Experimental.

*General Procedure.*—*m*- or *p*-Nitroaniline (2·6 g.) was dissolved in hot hydrochloric acid (*d* 1·6, 50 c.c.), and the solution cooled to room temperature, treated with finely powdered sodium nitrite (2 g.), and kept for 30 mins., diazotisation then

being complete. The metallic salt was then added, and the mixture gently boiled for 30 mins. under reflux, the vapours being led into water to collect any chloronitrobenzene carried over. The reaction mixture was then steam-distilled, the distillate kept at 0° to ensure that all the chloronitrobenzene had separated, aud the latter then removed, dried, and weighed. The second product of the decomposition reaction was in all cases identified qualitatively as the corresponding nitrophenol.

For the cobalt experiments with nitrosyl sulphate diazotisations, *p*-nitroaniline (2·6 g.), dissolved in glacial acetic acid (30 c.c.), was added to a solution of sodium nitrite (2 g.) in sulphuric acid (10 c.c., *d* 1·84), the mixture kept for 1 hour, and then poured into a solution of hydrated cobalt chloride (6 g.) in hydrochloric acid (100 c.c., *d* 1·16), which was then boiled for 30 mins. and worked up as above. The *p*-nitrophenol in the flask, after removal of *p*-chloronitrobenzene by steam, was estimated by conversion into 4-chloro-2 : 6-dibromophenol, and then found to account for *p*-nitroaniline not converted into *p*-chloronitrobenzene : 3·3 g. of dibromo-compound = 1·5 g. of *p*-nitroaniline; 1·2 g. of *p*-chloronitrobenzene = 1·05 g. of *p*-nitroaniline; total = 2·55 g. (cf. 2·6 g. initially taken).

Yields of *m*- and *p*- chloronitrobenzenes from the decompositions of diazotised *m*- and *p*-nitroanilines in bbiling hydrochloric acid (50 c.c., *d* 1·16) with additions of metallic chlorides as given below.

| Addition. | *p*-$C_6H_4Cl\cdot NO_2$, g. | *p*-$C_6H_4Cl\cdot NO_2$, % | *m*-$C_6H_4Cl\cdot NO_2$, g. | *m*-$C_6H_4Cl\cdot NO_2$, % |
|---|---|---|---|---|
| HCl (*d* 1·16) : blank | 1·6 | 54·4 | 1·4 | 47·3 |
| $AlCl_3$, hydrated (10·7 g.) | 1·8 | 60·7 | 1·6 | 54·4 |
| $SbCl_3$ (9 g.) | 1·1 | 37·1 | 0·9 | 31·6 |
| $CaCl_2$, anhyd. (4 g., and 20 g.) | 1·6 | 54·4 | 1·4 | 47·3 |
| $CrCl_3$ | 1·6 | 54·4 | — | — |
| $CoCl_2$, hydrated (6·0 g.) | 2·1 | 70·9 | 1·8 | 60·7 |
| $CoCl_2$, hydrated (6·0 g.), solution diluted with water until pink | 0·3 | 10·2 | — | — |
| Blank of above, without $CoCl_2$ | 0·3 | 10·2 | — | — |
| $Cu_2Cl_2$ (4·0 g.) | 2·3 | 77·6 | 2·0 | 67·5 |
| $CuCl_2$, hydrated (6·9 g.) | 2·3 | 77·6 | 2·0 | 67·5 |
| $FeCl_3$, anhyd. (6·5 g.) | 2·3 | 77·6 | 2·0 | 67·5 |
| $HgCl_2$ (10·0 g.) | 1·6 | 54·4 | — | — |
| $NiCl_2$, hydrated (6·0 g.) | 1·8 | 60·7 | — | — |
| $SnCl_4$, hydrated (14·0 g.) | 1·8 | 60·7 | — | — |
| $ZnCl_2$, anhyd. (5·5 g.) | 1·6 | 54·4 | 1·4 | 47·3 |

The authors thank I.C.I. (Dyestuffs) Ltd. for various gifts.

TECHNICAL COLLEGE, HUDDERSFIELD. [*Received, August 19th*, 1943.]

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## 10. *Thermodynamic Dissociation Constants of Hydroxy- and Alkoxy-benzoic Acids.*

By BRYNMOR JONES and J. C. SPEAKMAN.

The thermodynamic dissociation constants of *o*-, *m*-, and *p*-hydroxybenzoic acids, and of their methyl, ethyl, *n*-propyl, and *iso*propyl ethers have been measured in aqueous solution at 20° by an electrometric method. The results are discussed in terms of the various influences known to be operative in benzene derivatives.

DETAILED studies of the polar influence of alkoxy-groups on the reactivity of organic compounds have been made (Kindler, *Annalen*, 1926, **450**, 1; 1928, **454**, 278; Robinson and Smith, J., 1926, 392; Robinson, Clarke, and Smith, J., 1927, 2647; Blakey, McCombie, and Scarborough, J., 1926, 2963; Bradfield and Brynmor Jones, J., 1928, 1006, *et seq.*; *Trans. Faraday Soc.*, 1941, **37**, 726; Brynmor Jones, J., 1943, 430), but there is on record no parallel series of measurements, using modern methods, of their influence on the dissociation constants of acids and bases. In the aliphatic series the only available data are due to Palomaa (*Chem. Zentr.*, 1912, **2**, 596), who measured the effects of alkoxy-groups on the dissociation constants of saturated aliphatic acids by the conductivity method. His values, expressed as $pK$ (= $-\log_{10}K$), for the alkoxyacetic acids at 25° are given below. For comparison the accurate value for acetic acid (Harned and Ehlers, *J. Amer. Chem. Soc.*, 1932, **54**, 1350) is also included.

*Dissociation constants of alkoxyacetic acids* ($CH_2R\cdot CO_2H$).

| R = | H. | HO. | MeO. | EtO. | Pr$^\alpha$O. | Pr$^\beta$O. | Bu$^\alpha$O. | Bu$^\beta$O. |
|---|---|---|---|---|---|---|---|---|
| $pK$ ..... | 4·756 | 3·82 | 3·53 | 3·60 | 3·65 | 3·69 | 3·66 | 3·67 |

In the aromatic series measurements are almost wholly confined to the hydroxy- and methoxy-acids; recent available data (references cited by Dippy, *Chem. Rev.*, 1939, **25**, 206—208) expressed as $pK$ are summarised in the following table; Tait's value for *m*-ethoxybenzoic acid (J., 1943, 423) is also included : it is identical with that found in the present work. These measurements relate to aqueous solutions except those for the boric acids, which were made in 25% alcohol.

| R = | H. | OH. | | | OMe. | | | OEt. | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | *o*-. | *m*-. | *p*-. | *o*-. | *m*-. | *p*-. | *o*-. | *m*-. | *p*-. |
| $C_6H_4R\cdot CO_2H$ ..... | 4·20$_3$ | — | — | — | 4·09$_3$ | 4·08$_3$ | 4·47 | — | 4·17 | — |
| | 4·18 | 2·98 | 4·08 | 4·54 | 4·09 | 4·05 | 4·44 | — | — | — |
| $C_6H_4R\cdot CH{:}CH\cdot CO_2H$ ..... | 4·44 | 4·61 | 4·40 | — | 4·46 | 4·38 | 4·54 | — | — | — |
| $C_6H_4R\cdot B(OH)_2$ ..... | 4·71 | — | — | — | — | — | — | 5·04 | 4·52 | 6·17 |
| $C_6H_4R\cdot CH_2\cdot CO_2H$ ..... | 4·66 | — | — | — | 4·80 | 4·65 | 4·69 | — | — | — |

Thermodynamic dissociation constants have now been determined in aqueous solution at 20° for the three isomeric monohydroxybenzoic acids and for thirteen alkoxybenzoic acids.

## Experimental.

*Materials.*—Pure crystalline specimens of the *m*- and *p*-alkoxybenzoic acids were available from earlier studies of their rates of chlorination (J., 1928, 1006; 1935, 1874; 1939, 420; 1943, 430), and these were recrystallised from benzene immediately before use and thoroughly dried.

*o*-Methoxybenzoic acid was obtained by alkaline hydrolysis of the methyl ester, prepared, but not isolated, from methyl salicylate, sodium methoxide, and methyl iodide; crystallised from glacial acetic acid and from benzene, it melted at 101° (Cohen and Dudley, J., 1910, **97**, 1737, give m. p. 99—101°). The other *o*-alkoxybenzoic acids were obtained from the purified ethyl esters by hydrolysis, the esters being prepared from ethyl salicylate, sodium ethoxide, and the appropriate alkyl iodide. They were hydrolysed by heating under reflux with an excess of alcoholic sodium hydroxide for 45 minutes; and after removal of the alcohol the ice-cold alkaline solutions were acidified with 4N-sulphuric acid, the alkoxybenzoic acids separating as colourless oils. *o-n*-Propoxybenzoic acid, from ethyl *o-n*-propoxybenzoate (b. p. 147°/12 mm.), quickly solidified, and after two crystallisations from ethyl alcohol melted at 40° (Found: C, 66·7; H, 6·5. Calc.: C, 66·7; H, 6·7%); Cohen and Dudley (*loc. cit.*) record that the m. p. is low but give no definite value; Price, Salsbury, and Fredericksen (*J. Amer. Chem. Soc.*, 1942, **64**, 1691) record b. p. 205—207°. From the earlier work of Cohen and Dudley (who record m. p. 19—20°) *o*-ethoxybenzoic acid was known to be a liquid at room temperature, and special care was therefore taken in its purification. Ethyl *o*-ethoxybenzoate (b. p. 136°/10 mm.) was hydrolysed as above, and the acid liberated by the addition of 4N-sulphuric acid was extracted with ether. The extract was shaken repeatedly with an aqueous solution of sodium hydrogen carbonate, and the *o*-ethoxybenzoic acid liberated from the aqueous layer by the addition of more sulphuric acid was extracted with ether, washed, and dried. After removal of solvent it distilled as a colourless oil (b. p. 153—155°/0·2 mm.). It was further purified by freezing. *o-iso*Propoxybenzoic acid, similarly prepared from ethyl *o-iso*propoxybenzoate (b. p. 147°/13 mm.), distilled as a colourless liquid (b.p. 182°/18 mm.).

The benzoic acid was a commercially pure sample thrice crystallised from water.

*Method.*—Thermodynamic dissociation constants at 20° were determined by potentiometric titration, a glass electrode being used. The method was based on one previously described (J., 1940, 855); but for the present work the pH scale was standardised by experiments on benzoic acid, the p$K$ of which at 20° was taken to be 4·23—a value derived by interpolation from the accurate data of Rule and La Mer (*J. Amer. Chem. Soc.*, 1938, **60**, 1981). Dippy and Williams's conductivity measurements (J., 1934, 1888) would lead to a slightly lower value of p$K$.

*Results.*—These, expressed as p$K$, are given in the following table. Each value is based on at least four separate determinations. The accuracy, an estimate of which is shown for each acid, was limited mainly by the slight solubility, which prevented measurements on the higher members of the *m*- and *p*-series, and was the more troublesome in the latter. *p*-Ethoxybenzoic acid had a particularly low solubility (probably less than 0·0003M), which may be related to its high m. p. (cf. J., 1939, 420).

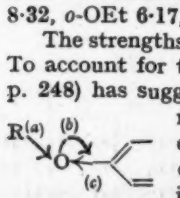
*Thermodynamic dissociation constants of alkoxybenzoic acids*, $C_6H_4R{\cdot}CO_2H$, at 20°.

| R. | | *o*-. | *m*-. | *p*-. |
|---|---|---|---|---|
| H | 4·23 | | | |
| HO | | 3·07 ± 0·02 | 4·19 ± 0·02 | 4·62 ± 0·03 |
| MeO | | 4·08 0·03 | 4·11 0·03 | 4·52 0·03 |
| EtO | | 4·21 0·03 | 4·17 0·04 | 4·80 0·10 |
| Pr$^{\alpha}$O | | 4·24 0·03 | 4·20 0·05 | 4·78 0·10 |
| Pr$^{\beta}$O | | 4·24 0·04 | 4·15 0·05 | 4·68 0·10 |
| Bu$^{\alpha}$O | | — | 4·25 0·05 | — |

By continuing the titration, the values of p$K_2$, corresponding to the secondary (phenolic) dissociation constants ($K_2$), of *m*- and *p*-hydroxybenzoic acid were found to be respectively 9·94 ± 0·03 and 9·39 ± 0·03. This constant of salicylic acid is too small to be easily measurable in water.

*Discussion.*—Although hydroxyl and alkoxyl groups linked to saturated carbon atoms or to the *m*-carbon atom of the benzene ring exhibit an attraction for electrons (− $I$ effect), an opposing mesomeric (+ $M$) effect (and in reactions an electromeric effect also) operates when the group is in the *p*-position of compounds such as benzoic or cinnamic acid. As a result, all *m*-substituted benzoic acids are stronger, and all *p*-substituted acids weaker, than the parent acid (cf. table). If these two effects were the only ones operating, then salicylic acid and all the *o*-alkoxybenzoic acids should also be weaker than benzoic acid. Instead, salicylic acid and *o*-methoxy- and *o*-ethoxy-benzoic acid are stronger, and the *o*-propoxybenzoic acids only a little weaker, than benzoic acid. The high dissociation constant of salicylic acid is generally attributed to chelation between the hydroxyl and the carboxyl group, a process which will occur more readily when the latter group is ionised and which will therefore stabilise the anion at the expense of the undissociated acid molecule (cf. Branch and Yabroff, *J. Amer. Chem. Soc.*, 1934, **56**, 2568). This explanation finds support in the further increase in strength which accompanies the introduction of a second hydroxyl, as in 2 : 6-dihydroxybenzoic acid, in which hydrogen bonds can be formed by both oxygen atoms of the carboxyl group (Baker, *Nature*, 1936, **137**, 236), and by the marked fall in strength which occurs when chelation is prevented by alkylation of the hydroxyl group in salicylic acid. The dissociation constants ($K \times 10^5$) fall in the following order; 2 : 6-(OH)$_2$ 5000, *o*-OH 85·1, *o*-OMe 8·32, *o*-OEt 6·17, *o*-OPr$^{\alpha}$ 5·75, *o*-OPr$^{\beta}$ 5·75.

The strengths of the *o*-alkoxybenzoic acids, however, are still higher than would be expected at first sight. To account for this in methoxybenzoic acid, Watson ("Modern Theories of Organic Chemistry," 2nd edn., p. 248) has suggested that the electron-attracting inductive effect (*c*) of methoxyl operating at close range more than balances the mesomeric effect (*b*) which is responsible for the low dissociation constant of anisic acid. If this be so, then the subsequent gradual fall in strengths in the order MeO > EtO > Pr$^{\alpha}$O = Pr$^{\beta}$O can be accounted for by the normal increase in the inductive effect (*a*) of alkyl groups assisting the mesomeric effect (*b*) of alkoxyl to overcome its inductive effect (*c*).



Certain features of the dissociation constants of the *m*- and *p*-alkoxybenzoic acids call for comment. (i) The increase in strength, found by earlier workers and confirmed now, which accompanies the replacement of hydroxyl hydrogen by methyl. This behaviour, also shown by the aliphatic acids (see table, p. 19), is contrary to expectation in that alkyl groups are normally regarded as electron repelling (cf. Dippy and Page, J., 1938, 358; Dippy, *ibid.*, p. 1324; Evans, Gordon, and Watson, *ibid.*, p. 1441, and references cited therein). The general tendency of hydroxyl and alkoxyl groups to strengthen an acid is to be attributed to the electron-attracting (inductive) power of the oxygen atom. It should be observed, however, that the $\overset{+}{H}–\overset{-}{O}$ dipole (as distinct from the dipole associated with the $\overset{-}{O}–\overset{+}{C}$ bond) is so directed that it has a resolved part which opposes the inductive effect and so tends to weaken the acid. The same influence is exerted by the Me–O dipole; but, in that this dipole is weaker (about 1·1 D.) than that of H–O (about 1·5 D.), it will weaken the acid to a less extent. In other words, when the hydrogen atom is replaced by alkyl, the negative ionic character of the oxygen atom is diminished, with a consequent increase in its inductive effect. In this way the enhanced strengths of the methoxy-acids in both aromatic and aliphatic series may perhaps be explained. Applying a suggestion of Ingold (*Chem. Rev.*, 1934, **15**, 238), Dippy (*loc. cit.*) accounts for the phenomenon by postulating that in methoxyl the methyl group, contrary to its normal habit, attracts electrons. This suggestion is in a sense covered by that given above: in that the moment of MeO is less than that of HO, methyl may be regarded as attracting electrons more than does hydrogen; more precisely, it responds to the electron attraction of the oxygen to a relatively smaller extent.

(ii) It is not so easy to understand the unexpected rise in strength resulting from a branching of the hydrocarbon chain: in both the *m*- and the *p*-series the *iso*propoxy- is stronger than the *n*-propoxy-benzoic acid.

(iii) Finally, when log *K* for these acids is plotted against the logarithm of the specific velocity of chlorination, an approximately linear relationship is shown (cf. Hammett, *Chem. Rev.*, 1935, **17**, 125; Bradfield and B. Jones, *loc. cit.*). The range of dissociation constants here is, however, too restricted to justify fuller discussion.

THE UNIVERSITY, SHEFFIELD, 10. [*Received, November 15th*, 1943.]

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## 11. *Reactions of 3-Nitro-1-naphthylamine, including Anil Formation, Bromination, and the Preparation of 1 : 2 : 3 : 4-Tetrabromonaphthalene.*

By HERBERT H. HODGSON and DAVID E. HATHWAY.

3-Nitro-1-naphthylamine readily condenses with aldehydes to form anils, and is di- and not mono-brominated by bromine in chloroform solution; elimination of the amino-group has been effected to give an almost quantitative yield of β-nitronaphthalene.

1 : 2 : 3 : 4-*Tetrabromonaphthalene* has been prepared.

ALTHOUGH 3-nitro-1-naphthylamine is readily mononitrated in the 2-position (Hodgson and Turner, J., 1943, 391), direct bromination in chloroform solution, whether with 1 or 2 equivs. of bromine, always produces 2 : 4-*dibromo*-3-*nitro*-1-*naphthylamine*. In this respect 3-nitro- differs from 5-nitro-1-naphthylamine, which is monobrominated in the 2-position (Hodgson and Turner, J., 1942, 723), a result which shows that the 5- exerts a greater direct inhibiting effect than the 3-nitro-group under comparable conditions. 3-Nitro-1-naphthylamine readily condenses with aldehydes to form stable anils. Elimination of the amino-group after diazotisation, and subsequent treatment by the alcohol–cuprous oxide procedure affords an almost quantitative yield of β-nitronaphthalene.

### EXPERIMENTAL.

(All m. p.'s are corrected.)

*Derivatives of 3-Nitro-1-naphthylamine.*—The *benzoyl* derivative, prepared by the Schotten–Baumann reaction in acetone, crystallised from alcohol in lemon parallelepipeds, m. p. 220° (Found: N, 9·6. $C_{17}H_{12}O_3N_2$ requires N, 9·6%). The *toluene-p-sulphonyl* derivative, prepared in pyridine solution, crystallised from alcohol in long, colourless needles, m. p. 200° (Found: N, 8·4. $C_{17}H_{14}O_4N_2S$ requires N, 8·2%).

NN′-*Diacetyl*-1 : 3-*naphthylenediamine* was obtained by reductive acetylation of 3-nitro-1-naphthylamine (1·8 g.) with zinc dust (3 g.) in a mixture of hot acetic anhydride (4 c.c.) and fused sodium acetate (1·6 g.). The hot filtered solutions deposited the diacetyl compound, which crystallised from glacial acetic acid in colourless parallelepipeds, m. p. 264° (Friedländer, *Ber.*, 1895, **28**, 1953, gives m.p. 263°) (Found: N, 11·5. Calc. for $C_{14}H_{14}O_2N_2$: N, 11·6%); yield, 0·4 g.

*Elimination of the amino-group.* 3-Nitro-1-naphthylamine (1·5 g.) was dissolved in glacial acetic acid (15 c.c.), stirred into a solution of sodium nitrite (0·9 g.) in sulphuric acid (10·5 c.c., *d* 1·84) below 20°, and the resulting diazonium solution treated with a mixture of cuprous oxide (1·5 g.) and ethyl alcohol (75 c.c.). After the reaction had ceased, the mixture was either steam-distilled, or diluted with 500 c.c. of water, filtered, and the solid extracted with alcohol (charcoal). Yield of β-nitronaphthalene, 1 g.; m. p. and mixed m. p. with authentic specimen, 79°.

*Anils.*—Stoicheiometric proportions of 3-nitro-1-naphthylamine and the aldehyde were dissolved separately in the minimal quantities of glacial acetic acid; the solutions were then mixed and refluxed. The anil separated on cooling and was recrystallised from glacial acetic acid. The *benzylidene* anil crystallised in small yellow plates, m. p. 122° (Found: N, 10·1. $C_{17}H_{12}O_2N_2$ requires N, 10·2%); the *o-nitrobenzylidene* anil, m. p. 194° (Found: N, 13·0. $C_{17}H_{11}O_4N_3$ requires N, 13·1%), the *m-isomer*, m. p. 188° (Found: N, 13·3%), and the *p-isomer*, m. p. 242° (sinters at 235°) (Found:

N, 13·2%), all crystallised in small, yellow parallelepipeds, and the p-*hydroxybenzylidene* anil in long, olive parallelepipeds, m. p. 233° (Found: N, 9·6. $C_{17}H_{12}O_3N_2$ requires N, 9·6%).

*Bromination of* 3-*Nitro*-1-*naphthylamine.*—*Attempted monobromination.* When 7 c.c. of a solution of bromine (1 c.c.) in dry chloroform (9 c.c.) were added to a solution of 3-nitro-1-naphthylamine (3 g.) in dry chloroform (20 c.c.), dropwise with stirring, at 40—50°, 2 : 4-dibromo-3-nitro-1-naphthylamine hydrobromide was precipitated; this was removed, basified with ammonia, and the free *amine* (*ca.* 2 g.) crystallised twice from ethyl alcohol (charcoal), forming small, bright yellow plates, m. p. 182° (Found: N, 8·4. $C_{10}H_6O_2N_2Br_2$ requires N, 8·1%). No monobromo-product could be detected.

*Dibromination.* When 18 c.c. of the above bromine–chloroform solution were employed, the yield of 2 : 4-dibromo-3-nitro-1-naphthylamine obtained was 3·5 g. (almost quantitative). Its *acetyl* derivative crystallised from acetic acid in colourless rhombs, m. p. 202° (Found: N, 7·1. $C_{12}H_8O_3N_2Br_2$ requires N, 7·2%).

*Some Halogeno-nitronaphthalenes and -naphthylamines.*—1 : 3-*Dibromo*-2-*nitronaphthalene.* A solution of 2 : 4-dibromo-3-nitro-1-naphthylamine (3 g.) in glacial acetic acid (20 c.c.) was stirred below 20° into one of sodium nitrite (0·8 g.) in sulphuric acid (10 c.c., *d* 1·84). After 30 mins., the diazonium solution was stirred into a suspension of cuprous oxide (1 g.) in ethyl alcohol (50 c.c.), and when the reaction had ceased the mixture was poured into ice-water (500 c.c.). The yellowish-white precipitate was filtered off and extracted with ethyl alcohol; from the filtered extract 1 : 3-*dibromo*-2-*nitronaphthalene* separated and, on recrystallisation from ethyl alcohol (charcoal), was obtained in slender, almost colourless parallelepipeds, m. p. 130·5° (Found: N, 4·4; Br, 48·0. $C_{10}H_5O_2NBr_2$ requires N, 4·2; Br, 48·3%); yield, 2 g.

1 : 3-Dibromo-2-naphthylamine was obtained when a solution of this nitro-compound (0·25 g.) in ethyl alcohol (12 c.c.) and water (4 c.c.) was refluxed with sodium hyposulphite (hydros, 0·75 g.) for 60 minutes; inorganic matter was filtered off, and the filtrate concentrated until it deposited long, colourless needles of the amine, m. p. 119·5° (Bell, J., 1932, 2733, gives m. p. 119°) (Found: N, 4·9. Calc.: N, 4·7%); yield, 0·2 g.

1 : 3 : 4-*Tribromo*-2-*nitronaphthalene* was obtained when 2 : 4-dibromo-3-nitro-1-naphthylamine (3·5 g.) was diazotised as above by Hodgson and Walker's method (J., 1933, 1620), and the diazonium solution decomposed by addition, below 20°, to a solution of cuprous bromide (1·5 g.) in hydrobromic acid (10 c.c., *d* 1·7). The tribromo-compound (4·0 g.) which separated crystallised from ethyl alcohol in cream parallelepipeds, m. p. 218° (Found: N, 3·6. $C_{10}H_4O_2NBr_3$ requires N, 3·4%).

1 : 3 : 4-*Tribromo*-2-*naphthylamine*, prepared from the previous nitro-compound (2 g.) by aqueous-alcoholic sodium hyposulphite reduction as above, was obtained in pale straw-coloured plates, m. p. 163° (Found: N, 4·0. $C_{10}H_6NBr_3$ requires N, 3·7%); yield, 1·2 g.

4-*Chloro*-1 : 3-*dibromo*-2-*nitronaphthalene* was prepared by decomposition of the diazonium sulphate from 2 : 4-dibromo-3-nitro-1-naphthylamine (1·5 g.) with a solution of cuprous chloride in hydrochloric acid (*d* 1·16); it separated from ethyl alcohol in almost colourless, spear-shaped crystals, m. p. 198° (Found: N, 3·9. $C_{10}H_4O_2NClBr_2$ requires N, 3·8%); yield, 0·8 g. The corresponding *amine*, obtained by aqueous-alcoholic sodium hyposulphite reduction, as above, of the nitro-compound (0·5 g.), crystallised from ethyl alcohol in fine white needles, m. p. 161° (Found: N, 4·3. $C_{10}H_6NClBr_2$ requires N, 4·2%); yield, 0·3 g.

*Preparation of* 1 : 2 : 3 : 4-*Tetrabromonaphthalene.*—The diazonium sulphate solution obtained from 1 : 3 : 4-tribromo-2-naphthylamine (1 g.) by Hodgson and Walker's procedure (*loc. cit.*) was decomposed by the cuprous bromide–hydrobromic acid mixture (as above) below 20°, and the whole poured into water; the precipitated brown 1 : 2 : 3 : 4-*tetrabromonaphthalene* crystallised from ethyl alcohol in rosettes of small, pale buff plates, m. p. 196° (Found: Br, 72·0. $C_{10}H_4Br_4$ requires Br, 72%); yield, 0·7 g.

The authors thank I.C.I. (Dyestuffs) Ltd. for gifts of chemicals.

TECHNICAL COLLEGE, HUDDERSFIELD. [*Received, August 19th*, 1943.]

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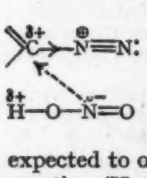
## 12. *The Replacement of the Diazonium by the Nitro-group. A General Method based on the Decomposition of the Aryldiazonium Cobaltinitrites.*

By HERBERT H. HODGSON and EWART MARSDEN.

Aryldiazonium *cobaltinitrites*, $(R\cdot\overset{\oplus}{N}_2)_3\{\overset{\ominus\ominus\ominus}{Co}(NO_2)_6$, have been prepared; they are immediately decomposed in the cold by aqueous sodium nitrite in the presence of cuprous oxide and cupric sulphate, and some even without the sulphate, to give excellent yields of aryl nitro-compounds. The reaction is held to indicate the presence of some nitrito-groups in the cobaltinitrite anion.

PREVIOUS work on the replacement of the diazonium by the nitro-group has been carried out by Sandmeyer (*Ber.*, 1887, **20**, 1495), Veselý and Dvorák (*Bull. Soc. chim.*, 1922, **31**, 421), Orton (J., 1903, **83**, 806), Bucherer and von der Recke (*J. pr. Chem.*, 1931, **132**, 121), Hantzsch and Blagden (*Ber.*, 1900, **33**, 2544; I.G., Anm. I. 485629), and Contardi (*Ann. Chim. Appl.*, 1923, **7**, 13). In every case, however, the reactions were of limited application (cf. Saunders, "The Aromatic Diazo-compounds and Their Technical Applications," 1936, p. 158).

Since diazonium nitrites decompose in nitrous acid solution to form nitro-compounds, the mechanism of the reaction would appear to be attack of the carbon atom to which the diazonium group is attached by anionoid nitrogen (due to resonance) of the nitrito-group (inset), otherwise attack by oxygen would form the hitherto unknown, and therefore very unstable, phenyl nitrite, of which the nitrite group must immediately isomerise into the stable nitro-group. This mechanism follows on the analogy of the much greater reactivity of anionoid nitrogen (due to resonance) in nucleophilic nitrous acid (cf. Kenner, *Chem. and Ind.*, 1941, **60**, 443) than of either of its oxygens for the kationoid carbon atom. Accordingly, complex salts with diazonium kations and metallic nitrito-anions were expected to offer a means of preparing nitro-compounds by a mechanism analogous to that of the Sandmeyer reaction (Hodgson, Birtwell, and Walker, J., 1941, 770).



For this purpose, the aromatic diazonium ***cobaltinitrites***, which have not hitherto been described, have been prepared. They are obtained in almost quantitative yield by the simple addition of sodium cobaltinitrite to a solution of a diazonium salt previously neutralised by calcium carbonate; they are yellow to orange crystalline substances which, when prepared from the nitro- and chloro-anilines, are stable when dry, but those from the toluidines, anisidines, and α-naphthylamine are less stable. On heating, however, the cobaltinitrites decompose, sometimes with explosive violence (*e.g.*, the complex from *p*-nitroaniline). They couple with β-naphthol in alkaline solution, and with α- and β-naphthylamine in acetic acid solution, but in hydrochloric acid they diazotise amines and nitrosate phenols by the nitrous acid formed during decomposition of the complex salt by the mineral acid.

When the solid diazonium cobaltinitrites from aniline, *o*-, *m*-, and *p*-nitroanilines and *p*-chloroaniline were added to a suspension of cuprous oxide in concentrated aqueous sodium nitrite, a vigorous evolution of nitrogen took place in the cold, and excellent yields of nitro-compounds were obtained. With the cobaltinitrites, however, from *o*- and *p*-toluidine, *o*- and *p*-anisidine, and α- and β-naphthylamine, the yields were poor, nor did the further addition of freshly precipitated copper effect any appreciable improvement; when copper sulphate was also present, however, all the diazonium cobaltinitrites as yet prepared decomposed to give yields above 60%. In the absence of sodium nitrite, cuprous oxide, either alone or in conjunction with copper sulphate, would not decompose the cobaltinitrite in the cold, although on heating there was a vigorous reaction without, however, the production of a nitro-compound; addition of sodium nitrite to the cold mixture immediately brought about formation of the relevant nitro-compound.

The results confirm the expectations noted above, the anionoid (nucleophilic) nitrito-group of the complex cobalt anion attacking the kationoid (electrophilic carbon atom of the diazonium compound. The simpler mechanism of nitrogen attack, however, would imply that the cobaltinitrite anion contained at least some of its nitrito-groups attached to the central cobalt atom by oxygen. This appears reasonable in view of the facts: (1) that the nitrito-groups in the metallic cobaltinitrites are indicated by magnetic data to be covalently linked (cf. Pauling, " Nature of the Chemical Bond," 1940, p. 116); (2) on analogy, the mixed inorganic cobalt complex salts containing both $NH_3$ and $NO_2$ groups are found in two forms, *viz.*, the red unstable nitritopentammine salts, *e.g.*, $[Co(NH_3)_5(ONO)]X_2$, and the more stable nitropentammines, *e.g.*, $[Co(NH_3)_5(NO_2)]X_2$ (cf. Emeléus and Anderson, " Modern Aspects of Inorganic Chemistry, 1943, pp. 84—86). Further, both $NH_3$ and $NO_2$ are themselves anionoid, but the introduction of $NH_3$ into the cobalt complex renders it kationoid, whereas the nitrito-group renders the complex anionoid. It is reasonable, therefore, to assume that reaction occurs *via* a feebly linked nitrito-group in view of the direct formation of a nitro-compound on the decomposition of a diazonium cobaltinitrite. The function of the copper compounds is to bring about the elimination of the diazonium nitrogen (cf. Sandmeyer, *loc. cit.*, and Contardi, who concluded that cupric were as effective as cuprous salts), and the rôle of the sodium nitrite would appear to be the re-formation of stable sodium cobaltinitrite, which would in consequence be the main driving force of the decomposition, since the copper compounds did not themselves effect reaction in the cold.

The excellent yields of nitro-compounds, together with the facile preparation of the intermediate diazonium cobaltinitrites, indicate this new replacement method to be of general application.

## Experimental.

*Preparation and Analysis of Aromatic Diazonium Cobaltinitrites.*—The amine (0·1 g.-mol.) is diazotised in either hydrochloric or sulphuric acid solution with sodium nitrite (7 g.), the volume of liquid being kept as small as possible. The diazonium solution is neutralised with calcium carbonate and filtered; finely powdered sodium cobaltinitrite (15 g.) is stirred into the filtrate, and the crystalline aryldiazonium cobaltinitrite, which separates rapidly, is filtered off, air-dried, and analysed by coupling 0·5 g. of it with β-naphthol; the resulting azo-compound is filtered off, washed with cold alcohol and water on the filter until free from β-naphthol, then with hot dilute hydrochloric acid until free from cobalt salts, and finally with water, after which it is dried, and weighed.

*Replacement of the Diazonium by the Nitro-group.*—The finely powdered cobaltinitrite (10 g.) is added portionwise at room temperature to a well-stirred solution of sodium nitrite (10 g.) and crystallised copper sulphate (10 g.) in water (60 c.c.) in which cuprous oxide (4 g.) is suspended. After the evolution of nitrogen, which at the outset is somewhat vigorous, is complete (sometimes only after standing overnight), the resulting nitro-compound is removed by steam (when volatile) or by extraction with a suitable solvent (*e.g.*, chloroform). Before steam distillation, the reaction mixture should be made alkaline with sodium hydroxide.

*Some Aryldiazonium Cobaltinitrites.*

| Amine diazotised. | Colour of the cobaltinitrite. | Yield, g. | Yield, % | Arylazo-β-naphthol. Obtained, g. | Yield, % |
|---|---|---|---|---|---|
| Aniline | Light orange | 19·2 | 88·5 | 0·5703 | 99·6 |
| *o*-Nitroaniline | Orange | 26·0 | 99·0 | 0·5581 | 99·7 |
| *m*-Nitroaniline | Orange | 22·3 | 89·9 | 0·5584 | 99·7 |
| *p*-Nitroaniline | Orange | 19·5 | 74·5 | 0·5570 | 99·5 |
| *p*-Chloroaniline | Orange | 21·2 | 84·0 | 0·5644 | 100·3 |
| α-Naphthylamine | Dark orange | 21·8 | 81·6 | 0·5598 | 100·2 |
| β-Naphthylamine | Yellow | 26·5 | 99·0 | 0·5600 | 100·2 |

[The yield of arylazo-β-naphthol is given as a percentage of that to be expected from the reaction $(RN_2)_3Co(NO_2)_6 \longrightarrow 3R{\cdot}N_2{\cdot}C_{10}H_6{\cdot}OH$.]

*Decomposition of Aryldiazonium Cobaltinitrites* (10 g.) *to Nitroaryls.*

| Amine diazotised. | Product. | Yield, g. | Yield, % |
|---|---|---|---|
| (*a*) By cuprous oxide only. | | | |
| Aniline | Nitrobenzene | 4·3 | 75·5 |
| *o*-Nitroaniline | *o*-Dinitrobenzene | 4·3 | 67·4 |
| *m*-Nitroaniline | *m*-Dinitrobenzene | 4·6 | 72·0 |
| *p*-Nitroaniline | *p*-Dinitrobenzene | 4·8 | 75·0 |
| *p*-Chloroaniline | *p*-Chloronitrobenzene | 5·2 | 82·5 |
| α-Naphthylamine | α-Nitronaphthalene | 1·3 | 20·0 |
| β-Naphthylamine | β-Nitronaphthalene | 1·1 | 16·9 |
| (*b*) By cuprous oxide–copper sulphate. | | | |
| α-Naphthylamine | α-Nitronaphthalene | 4·4 | 68·0 |
| β-Naphthylamine | β-Nitronaphthalene | 3·9 | 60·0 |
| *p*-Toluidine | *p*-Nitrotoluene | 4·1 | 69·0 |
| *p*-Anisidine | *p*-Nitroanisole | 4·2 | 68·0 |
| (*c*) By cuprous oxide–copper sulphate, but yield based on weight of amine (5 g.) taken.* | | | |
| *o*-Toluidine | *o*-Nitrotoluene | 3·9 | 61·0 |
| *o*-Anisidine | *o*-Nitroanisole | 3·9 | 63·0 |

* These cobaltinitrites were less stable than the others, and so were not dried, but washed with water and immediately decomposed as above; hence the yields have to be calculated on the amount of amine diazotised.

The authors thank I.C.I. (Dyestuffs) Ltd. for gifts of chemicals.

TECHNICAL COLLEGE, HUDDERSFIELD. [*Received, August 26th*, 1943.]

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## 13. *Preparation of Nitroethane.*

By H. MCCOMBIE, B. C. SAUNDERS, and F. WILD.

A convenient method for the preparation of nitroethane on a laboratory scale is described.

ALTHOUGH nitroethane can be satisfactorily prepared on a technical scale by nitrating ethane (*e.g.*, Hodge, U.S. 2,150,120, 1939), nodetails have been recorded for its preparation in quantity on a laboratory scale by a relatively inexpensive method. The preparation from silver nitrite and ethyl iodide is obviously too expensive. The same drawback applies to the reaction between α-bromopropionic acid and sodium nitrite (50% yield), particularly since lactic acid was found by us to give only a 13% yield of α-bromopropionic acid on treatment with hydrogen bromide. Very little α-chloropropionic acid is produced by the action of hydrogen chloride on lactic acid.

Kaufler and Pomeranz (*Monatsh.*, 1901, **22**, 492) showed that methyl sulphate and aqueous potassium nitrite reacted to give a 25% yield of nitromethane. Walden (*Ber.*, 1907, **40**, 3214) obtained a 50—57% yield by a similar method, and stated that ethyl sulphate also reacted, but less energetically. However he gave neither yield nor details of the latter reaction. The reaction between aqueous sodium nitrite and ethyl sulphate has now been investigated in detail. In the procedure recommended, there is no loss due to the slight solubility of nitroethane in water. All the yields recorded below are based on the equation:

$$EtO{\cdot}SO_2{\cdot}OEt + NaNO_2 = EtO{\cdot}SO_2{\cdot}ONa + EtNO_2$$

This raises the question of the utilisation of the sodium ethyl sulphate produced in the reaction. Krause (D.R.-P. 294,755, 1916) showed that this salt, when made into a cream with solid sodium nitrite, sodium carbonate, and a small quantity of water and distilled above 100°, gave a 35% yield of nitroethane. Accordingly the aqueous layer from reaction in the cold (initial reaction) was refluxed for 30 minutes with sodium carbonate and then distilled, but very little nitroethane was obtained. However, after a series of runs in the cold, crystalline sodium ethyl sulphate separated from the standard solution, and could then be worked up according to the method of Krause. In this way the yield of nitroethane was increased above the 65% recorded below.

A series of experiments was also carried out varying (*a*) the concentration of sodium nitrite solution used, (*b*) the actual amount of sodium nitrite used. It was found that, within limits, the more dilute the solution, the greater the production of nitrous fumes and ethyl nitrite at the expense of nitroethane. The optimum concentration was 75 g. of sodium nitrite dissolved in 100 c.c. of water. With concentrations greater than this (saturated solution plus solid) the yield was considerably reduced, probably because less water was used and therefore the surface area available for the reaction was less.

### EXPERIMENTAL.

*Initial Run.*—Into each of seven stoppered bottles was placed a mixture of ethyl sulphate (120 g.) and sodium nitrite solution (120 g. in 160 c.c. of water.) The bottles were shaken mechanically for 20 hours, the pressure being released at

intervals. The contents were then poured into a separating funnel, and the upper layer separated, dried over calcium chloride, and distilled at 14 mm., the distillate up to 60° being collected (the residue, *ca.* 230 g., consisted of ethyl sulphate and was used again). The distillate was fractionated at atmospheric pressure, and the fraction of b. p. 114—116° collected. This was shaken with water, dried over calcium chloride, run through charcoal, and redistilled; b. p. 114—115·5°. Yield, 124 g. (31%, or allowing for recovered ethyl sulphate, 43·5%) (Found: N, 18·4. Calc. for $C_2H_5O_2N$: N, 18·7%).

*Routine Run.*—A second experiment was then carried out using the same quantities of ethyl sulphate as above. The recovered nitrite solution (lower layer) from the first run was concentrated by adding approximately 16 g. of sodium nitrite per 160 c.c. of solution. Yield, 185 g. (46%, or allowing for recovered ethyl sulphate, 65%).

For each additional subsequent run approximately 16 g. of nitrite per 160 c.c. of solution were added, although this represents a rather diminishing concentration in view of the increased yield of nitroethane.

The table summarises experiments carried out under various conditions.

| Expt. | $Et_2SO_4$, g. | $NaNO_2$, g. | $H_2O$, c.c. | $NaNO_2$ per 100 g. $Et_2SO_4$. | C.c. $H_2O$ per 100 g. $Et_2SO_4$. | Nitroethane, g. | Recovered $Et_2SO_4$, g. | Pressure. |
|---|---|---|---|---|---|---|---|---|
| Sat. $NaNO_2$ plus solid ... | 100 | 100 | 50 | 100 | 50 | 4·89 | 72·5 | Nil |
| Dilute $NaNO_2$ ..... | 60 | 60 | 600 | 100 | 1000 | 2 | 8·6 | Considerable |
| Excess conc. $NaNO_2$ ..... | 100 | 150 | 187 | 150 | 187 | 11·5 | 56 | V. small |
| Intermediate conditions | 100 | 100 | 125 | 100 | 125 | 10 | 67 | Small |

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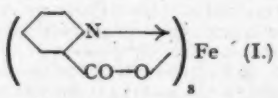
## 14. *Iron Derivatives of Heterocyclic Acids. Part I. Ferric Complexes of Chelidamic Acid.*

By JOHN H. GORVIN.

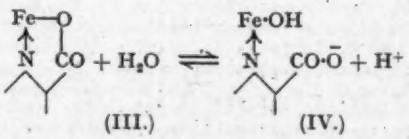
Brownlee, Bainbridge, and Thorp (*Quart. J. Pharm.*, 1942, **15**, 148) have established the value as hæmoglobin producers of certain ferric chelidamate derivatives prepared in these laboratories. These substances are neutralisation products of *dichelidamatoferric acid*, which contains one free and one masked carboxyl group, and gives rise to two series of water-soluble salts. The light-absorption of these complexes has been studied. Structural formulæ are assigned to them and to their insoluble *silver* and *iron* derivatives. The study is being extended to related derivatives of other pyridine-$\alpha\alpha'$-dicarboxylic acids.

A PRELIMINARY survey of ferric derivatives of pyridine-α-carboxylic acids has shown that either two or three molecules of picolinic acid may react with an atom of ferric iron. *Tripicolinatoiron* (I) (compare the analogous cobaltic complex of Ley and Ficken, *Ber.*, 1917, **50**, 1133) is readily formed from the acid and ferric hydroxide, and a compound of the type $(Acid)_2FeOH$ (II) has been described by Ley, Schwarte, and Münnich (*Ber.*, 1924, **57**, 355).

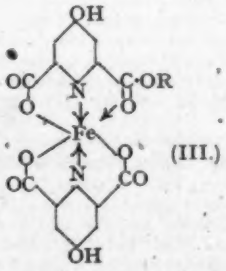
In substituted picolinic acids, spatial considerations favour formation of the smaller molecule; thus, 4-chloropicolinic acid forms only a *complex* of type (II) with ferric hydroxide. The case of chelidamic acid is similar, with the additional factor of elimination of the hydroxo-group by ring closure. Crystalline *dichelidamatoferric acid* has been assigned an octahedral structure (III; R = H), requiring a six-co-ordinate iron atom associated with two tridentate acid molecules in right-angular planes (compare Morgan and Burstall, J., 1937, 1649), with one strongly acidic carboxyl group available for salt formation. The acid has a p$K$ value of approximately 1·6 in 0·01M-solution.




(I.)



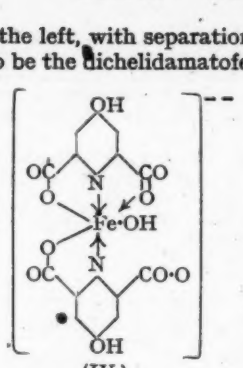

(III.) (IV.)



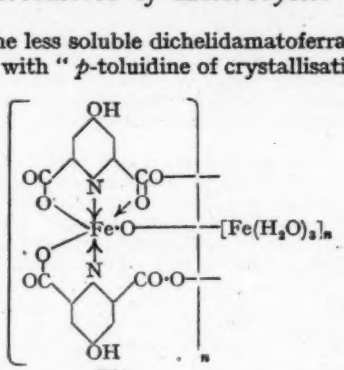

(III.)

The crystalline *dichelidamatoferrates* (III; R = kation) give orange-coloured aqueous solutions in which they behave as weak acids (p$K$ = 4·0 in 0·01M-solution); the colour intensity of the solutions is almost independent of concentration over a wide range. These effects can be explained by the partial opening of a five-membered ring, setting up the equilibrium (III) ⇌ (IV). These acidic salts, on neutralisation, give solutions containing the dichelidamatohydroxoferrate ion (IV), the intense blood-red colour of which is attributed to resonance in the ring system containing the strongly polarising iron atom. The highly soluble dichelidamatohydroxoferrates have not been obtained crystalline; for, in concentrated solutions, the equilibrium usually

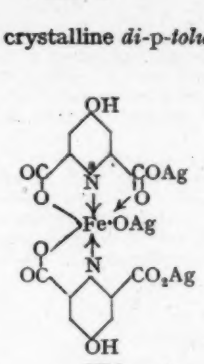
moves to the left, with separation of the less soluble dichelidamatoferrate. The crystalline *di*-p-*toluidine* salt appears to be the dichelidamatoferrate with " *p*-toluidine of crystallisation."



(IV.)



(V.)



(VI.)

The formation of dichelidamatohydroxoferrates is usually accompanied by some decomposition of the anion by the added base; the liberated ferric hydroxide combines with unchanged anion to give an insoluble *ferric* derivative (V; the value of $n$ is uncertain), also slowly formed by the action of ferric ions on dichelidamatoferric acid and its salts.

Dichelidamatohydroxoferrate solutions, filtered to remove ferric complex, remain stable at temperatures up to 100°. Unless there is crystallisation of dichelidamatoferrate, they are unchanged on evaporation, and finally give deep red scales, or, in the case of the *nor*-d-*ψ-ephedrine* compound, a highly soluble red powder shown by analysis to be analogous to the di-*p*-toluidine salt. Their aqueous solutions react immediately with silver ions to form the insoluble *trisilver dichelidamato-oxoferrate* (VI), in contrast to dichelidamatoferrate solutions which give mainly *silver dichelidamatoferrate* (III; R = Ag).

The substitution of iron and silver in the hydroxo-group, which appears to occur in compounds (V) and (VI), may be compared with the intermolecular condensation of $Fe(OH)_3$ to ortho-ferric hydroxide $(FeO_2H)_4$, and with the formation of silver ferrite $Ag_3H(FeO_2)_4$ by substitution in the active hydroxo-groups of this complex (Krause, *Ber.*, **1936**, **69**, 1982).

Evidence that the dichelidamatohydroxoferrate ion (IV) has a definite existence in aqueous solution is provided by light-absorption curves plotted at several dilutions, which indicate that solutions of the bistriethanolamine salt substantially obey Beer's law over the range of dilution 0·000025—0·0025M. The presence of an extra mol. of base does not radically affect the absorption, but, as (IV) is in equilibrium with (III) in solutions of dichelidamatohydroxoferrates of weak bases, the resulting pH increase may lead to a somewhat higher concentration of the strongly absorbing ion (IV) (compare the curves for 0·00025M-solutions). The curves supply no evidence for any ionisation of the hydroxo-group, but dichelidamatohydroxoferrates of strong bases were not studied in this connection, owing to the considerable decomposition which occurs in their preparation.

In the case of *ammonium dichelidamatoferrate* (III; R = $NH_4$), the increased ring-opening on dilution is accompanied by relative intensification of absorption in the blue-green region, and at 0·000025M-dilution, the form of the curve resembles that of the dichelidamatohydroxoferrates. The absorption of dichelidamatoferric acid, although similarly dependent on concentration, is always weaker than that of its salts at corresponding dilution, as ring opening is largely suppressed by hydrions from the free carboxyl group.

## Experimental.

Analytical figures for the following compounds were determined after drying at 120° in a vacuum; the loss in weight of the desiccator-dried substance is given as molecules of water of crystallisation. Hydrated crystals became opaque on drying, but no marked colour changes occurred. Unless otherwise stated, the compounds were stable up to 300° and insoluble in organic solvents. They were decomposed by excess of strong acids or alkalis.

*Tripicolinatoiron* (I).—Freshly prepared ferric hydroxide (1 mol.) was dissolved in a hot aqueous solution of picolinic acid (3·5 mols.). *Tripicolinatoiron* separated rapidly in yellow, crystalline flakes ($1H_2O$), insoluble in water, decomposing at 282° (corr.) (Found: C, 50·1; H, 3·0; N, 10·0; Fe, 13·4. $C_{18}H_{12}O_6N_3Fe$ requires C, 51·2; H, 2·9; N, 10·0; Fe, 13·2%).

*Di-(4-chloropicolinato)hydroxoiron.*—Prepared by analogous procedure from 4-chloropicolinic acid (Graf *et al.*, *Ber.*, 1931, **64**, 22), this *complex* formed a yellow, crystalline powder, insoluble in water; it darkened at 260—270° (Found: C, 37·3; H, 1·8; N, 7·4. $C_{12}H_7O_5N_2Cl_2Fe$ requires C, 37·3; H, 1·8; N, 7·3%).

*Dichelidamatoferric Acid* (III, R = H).—A suspension of ferric hydroxide (1·05 mols.) in water (10 l.) was boiled with chelidamic acid (2 mols.) and the solution then left overnight. After insoluble material had been filtered off, the orange-yellow solution was scratched to initiate crystallisation, giving *dichelidamatoferric acid* as a fine golden crystalline powder ($2H_2O$). The crop was filtered without delay, as insoluble impurity slowly separated from concentrated solutions of the acid (Found: C, 39·8; H, 1·9; N, 6·8; Fe, 13·2. $C_{14}H_7O_{10}N_2Fe$ requires C, 40·1; H, 1·7; N, 6·7; Fe, 13·3%).

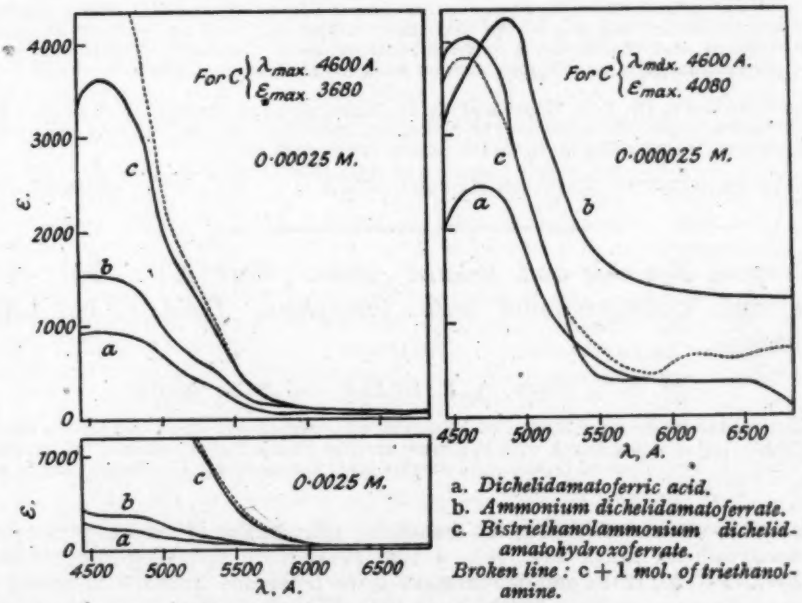
*Salts of Dichelidamatoferric Acid.*—These salts were prepared, either by adding 1·1 equivs. of the appropriate base, dissolved in water or alcohol, to a warm aqueous solution of the acid (1 mol.) (method I), or by treating an aqueous solution of ammonium dichelidamatoferrate (see below) with a soluble salt of the base (method II). The salts were recrystallised from water in each case.

*Ammonium salt.* Prepared by method I, or by treating strontium chelidamate with ferric ammonium sulphate, the *ammonium* salt formed yellow-green crystals ($2·5H_2O$) (Found: C, 38·9; H, 2·4; N, 9·6; Fe, 12·9. $C_{14}H_{16}O_{10}N_2Fe$ requires C, 38·5; H, 2·3; N, 9·6; Fe, 12·8%). This salt was referred to by Brownlee *et al.* (*loc. cit.*) as iron mono-ammonium chelidamate.

*Tetraethylammonium salt* (method I), olive-green rods ($2H_2O$) (Found: N, 7·7; Fe, 10·0. $C_{22}H_{26}O_{10}N_2Fe$ requires

N, 7·7; Fe, 10·2%). *o-Toluidine* salt (method I), brown crystals with gold reflex (Found: C, 47·9; H, 3·0; Fe, 10·6. $C_{21}H_{16}O_{10}N_3Fe$ requires C, 47·9; H, 3·1; Fe, 10·6%). *Pyridine* salt (method I), golden-yellow flakes (Found: C, 45·9; H, 2·4; Fe, 11·3. $C_{15}H_{13}O_{10}N_3Fe$ requires C, 45·8; H, 2·4; Fe, 11·2%). *Quinoline* salt (method I), flat yellow needles (Found: C, 50·3; H, 2·7; Fe, 10·2. $C_{23}H_{14}O_{10}N_3Fe$ requires C, 50·4; H, 2·6; Fe, 10·2%). *Quinine* salt (method I or II), small lemon-yellow needles, sparingly soluble in hot water (Found: C, 49·3; H, 3·6; N, 7·3; Fe, 9·5. $C_{48}H_{38}O_{22}N_6Fe_2$ requires C, 49·6; H, 3·3; N, 7·2; Fe, 9·6%). *Sodium* salt (method I), green crystals ($2H_2O$) (Found: C, 38·1; H, 1·7; N, 6·4. $C_{14}H_6O_{10}N_3FeNa$ requires C, 38·1; H, 1·4; N, 6·4%). *Potassium* salt (method I), yellow-green crystals ($2H_2O$) (Found: C, 37·1; H, 1·4; N, 6·2. $C_{14}H_6O_{10}N_3FeK$ requires C, 36·8; H, 1·3; N, 6·1%). *Silver* salt (method II), orange-yellow crystalline powder ($2H_2O$) sparingly soluble in hot water (Found: C, 31·7; H, 1·3; N, 5·4. $C_{14}H_6O_{10}N_3FeAg$ requires C, 31·9; H, 1·2; N, 5·3%). *Barium* salt (method I or II), yellow brown prisms ($2·5\ H_2O$), efflorescing in air (Found: C, 34·9; H, 1·4; N, 5·9. $C_{28}H_{12}O_{20}N_4Fe_2Ba$ requires C, 34·5; H, 1·2; N, 5·8%).

*The Dichelidamatohydroxoferrates* (IV).—Neutralisation of dichelidamatoferric acid with 2 mols. of a base, or of a dichelidamatoferrate with 1 mol., yielded an intense blood-red solution of a dichelidamatohydroxoferrate. Simultaneously the anion underwent decomposition to an extent depending on the strength of the added base, with separation of a fine precipitate of triaquoferric dichelidamato-oxoferrate (see below) and liberation of an equivalent amount of chelidamate ion in the solution. Separation of the insoluble complex was usually complete after leaving overnight; it was removed from the solution by filtration through kieselguhr. The formation of the diammonium salt (the iron diammonium chelidamate of Brownlee *et al.*, *loc. cit.*) and of the disodium and dipotassium salts was accompanied by appreciable decomposition of the anion, and evaporation of the solutions to dryness gave deep red scales of indefinite composition, highly soluble in water. On allowing the concentrated solution to stand, crystallisation of dichelidamatoferrate occurred, with decrease in the intensity of the colour. Complete conversion into the dichelidamatoferrate was achieved by dehydrating the solid scale with alcohol, or by passing sulphur dioxide through its aqueous solution.




a. *Dichelidamatoferric acid.*
b. *Ammonium dichelidamatoferrate.*
c. *Bistriethanolammonium dichelidamatohydroxoferrate.*
*Broken line:* c + 1 *mol. of triethanolamine.*

*Effect of dilution on light-absorption of the complexes.*

The bistriethanolamine salt (the iron triethanolamine chelidamate of Brownlee *et al.*, *loc. cit.*), prepared with only slight decomposition, gave a red scale on evaporation, with no tendency to crystallisation. The substance in aqueous solution passed readily through a collodion membrane.

The dipyridine salt was formed without any decomposition of the anion, but pyridinium dichelidamatoferrate began to crystallise almost immediately, with fading of the deep red colour. Addition of excess pyridine lessened, but did not entirely inhibit, the crystallisation. A similar, but less rapid, effect occurred in the case of the di-*o*-toluidine salt.

*Di-p-toluidine salt.* On addition of *p*-toluidine (0·54 g., 2 mols.), dissolved in alcohol, to a solution of dichelidamatoferric acid (1 mol.), a deep red solution was formed, which deposited a trace of insoluble material on standing. Filtration and concentration to 20 c.c. caused separation of orange-brown leaflets ($1H_2O$) of the *di-p-toluidine* salt, decomposing at 220—225°, soluble in hot water to a deep red solution (Found: C, 52·4; H, 4·1; N, 9·0; Fe, 8·9. $C_{21}H_{16}O_{10}N_3Fe$, $C_7H_9N$ requires C, 53·1; H, 4·0; N, 8·9; Fe, 8·8%).

*Dinor-d-ψ-ephedrine salt.* The deep red solution, prepared by the above method, using 2·1 mols. of nor-*d*-ψ-ephedrine, was evaporated to dryness and dried at 120° in a vacuum. The *salt* formed a red powder, very soluble in water and in alcohol (Found: C, 53·2; H, 4·7; N, 7·9; Fe, 7·8. $C_{23}H_{20}O_{11}N_3Fe,C_9H_{13}ON$ requires C, 53·3; H, 4·6; N, 7·8; Fe, 7·7%).

*Trisilver Dichelidamato-oxoferrate* (VI).—A 5% aqueous solution of silver nitrate was added in excess to a solution of bistriethanolammonium dichelidamatohydroxoferrate. A fine purple precipitate formed in the cold, but was brown and less finely divided in the hot. The dry *silver* derivative was a dark purple-brown powder, insoluble in water (Found: C, 22·5; H, 0·8; N, 3·7; Fe, 7·4; Ag, 42·6. $C_{14}H_4O_{11}N_3FeAg_3$ requires C, 22·2; H, 0·8; N, 3·7; Fe, 7·4; Ag, 42·7%).

*Triaquoferric Dichelidamato-oxoferrate* (V).—A suspension of ferric hydroxide (1 mol.) was treated with aqueous dichelidamatoferric acid (1·2 mols.), and the solution heated on the water-bath for 3 hours. The *ferric* derivative separated as a golden-brown mass of rod-shaped, yellow crystals ($4H_2O$), insoluble in water (Found: C, 31·1; H, 2·2; N, 5·3; Fe, 20·6. $C_{14}H_6O_{11}N_3Fe_2,3H_2O$ requires C, 30·9; H, 2·2; N, 5·2; Fe, 20·5%). The same compound was obtained as an orange-red powder (approx. $2H_2O$) by treating ammonium dichelidamatoferrate solution with ferric chloride, or by

filtering and washing the precipitate obtained during the preparation of dichelidamatohydroxoferrates of strong bases (see above).

*Acid Dissociation Constants for the Dichelidamatoferrates.*—The figures were calculated from the pH values of solutions of the ammonium and potassium salts at several dilutions, measured on a standard Cambridge pH meter. Solutions were made in boiled distilled water from known amounts of the recrystallised salt, dried to constant weight at 120° in a vacuum.

| | Molarity. | pH (11·5°). | $K_a \times 10^4$. | $pK_a$. | | Molarity. | pH (11·5°). | $K_a \times 10^4$. | $pK_a$. |
|---|---|---|---|---|---|---|---|---|---|
| $NH_4$ salt | 0·0125 | 3·00 | 0·87 | 4·06 | K salt | 0·0125 | 2·97 | 1·01 | 4·00 |
| ,, | 0·0100 | 3·05 | 0·87 | 4·06 | ,, | 0·0100 | 3·03 | 0·96 | 4·01 |
| ,, | 0·0083 | 3·09 | 0·88 | 4·06 | ,, | 0·0083 | 3·06 | 1·02 | 3·99 |

*First Dissociation Constant for Dichelidamatoferric Acid.*—Owing to the difficulty of obtaining an absolutely pure specimen of the crystalline acid, a known concentration of the pure acid was prepared in solution by dissolving ferric hydroxide in a slight excess of chelidamic acid, then removing the excess by the addition of half the previous quantity of ferric hydroxide. The insoluble ferric complex, which crystallised overnight, was filtered off and dried to constant weight. The known iron content of the complex gave a figure for the iron remaining in the dichelidamatoferric acid solution, which was then diluted to the required concentrations ($K_1 = 1{\cdot}0 \times 10^{-4}$).

| Molarity. | pH (15°). | $K_1 \times 10^3$. | $pK_1$. | Molarity. | pH (15°). | $K_1 \times 10^3$. | $pK_1$ |
|---|---|---|---|---|---|---|---|
| 0·0112 | 2·06 | 2·9 | 1·54 | 0·0077 | 2·20 | 2·6 | 1·58 |
| 0·0095 | 2·13 | 2·5 | 1·60 | | | | |

*The Absorption Curves.*—These were constructed from readings of percentage transmission and wave-length of light obtained on a wave-length monochrometer using a selenium " barrier-layer " type cell. Aqueous solutions of dichelidamatoferric acid and its ammonium salt, and of the bistriethanolamine salt, with and without an additional mol. of triethanolamine, were prepared, and diluted to the required concentrations. In 0·0025M-solution, the transmission in the blue-green region by the triethanolamine solutions was too weak for accurate readings to be taken.

The author's thanks are due to Dr. T. A. Henry and Mr. H. Paget, whose preliminary work on injectable iron solutions suggested this investigation, to Dr. Brownlee for the absorption measurements, to Mr. D. T. Warren for experimental assistance, and to Messrs. A. Bennett and H. C. Clarke for the micro-analyses.

WELLCOME BUREAU OF SCIENTIFIC RESEARCH, LONDON, N.W.1. [*Received, October 9th*, 1943.]

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## 15. *The Triterpene Resinols and Related Acids. Part XV. The Dehydration of α-Amyrin and α-Amyradienol with Phosphoric Oxide:* l-α-*Amyradiene and* l-α-*Amyratriene.*

By E. S. EWEN, A. E. GILLAM, and F. S. SPRING.

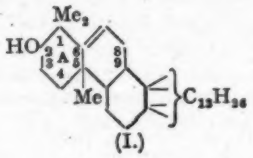
*l*-α-Amyradiene obtained by dehydration of α-amyrin with phosphoric oxide contains a conjugated diene system. Dehydration of α-amyradienol with the same reagent yields l-α-*amyratriene*, which contains a conjugated triene system. The ethenoid linkage of α-amyrin must consequently be situated in the vicinity of the hydroxyl group.

THREE α-amyradienes have been described in the literature; dehydration of α-amyrin with phosphorus pentachloride gives *d*-α-amyradiene, m. p. 134°, $[\alpha]_D$ + 109° (Vesterberg and Westerlind, *Annalen*, 1922, **428**, 250; Vesterberg, *Ber.*, 1887, **20**, 1245), and dehydration of the triterpene alcohol with phosphoric oxide yields the isomeric *l*-α-amyradiene, m. p. 193—194°, $[\alpha]_D$ − 105° (Vesterberg, *Ber.*, 1891, **24**, 3835). The third α-amyradiene, m. p. 119—120°, $[\alpha]_D$ + 137°, was obtained by Winterstein and Stein (*Annalen*, 1933, **502**, 223) by the thermal decomposition of α-amyrin benzoate. We have examined the ultra-violet absorption spectra of the three α-amyradienes and we find that, whereas the two *d*-isomers do not exhibit selective absorption of any appreciable intensity above 2200 A., the *l*-isomer exhibits intense selective absorption with a maximum at 2395 A. ($\varepsilon_{max.}$ = 15,000), showing that the hydrocarbon contains a conjugated system of ethenoid linkages distributed between two rings and that the ethenoid linkage of α-amyrin is in close proximity to the hydroxyl group.

The simplest structural interpretation of this observation is that the ethylenic linkage of α-amyrin is located between $C_6$ and $C_7$ (I) in the hydropicene nuclear structure, and that *l*-α-amyradiene is represented by the partial formula (II). This relative location of the unsaturated centre and hydroxyl group in the α-amyrin group of triterpenes, which is attractive since it corresponds to that in the more abundantly occurring zoosterols and phytosterols, has been suggested by Simpson and Williams (J., 1938, 1712; Ruzicka and Wirz, *Helv. Chim. Acta*, 1939, **22**, 948; Simpson and Kon, J., 1941, 793). If the ethylenic linkage of α-amyrin is between $C_6$ and $C_7$, an angular methyl group cannot be attached to $C_5$, since the reversible transformation of α-amyrenonol (III) into α-amyradienol (V) requires the presence of a hydrogen at $C_9$ (Ewen and Spring, J., 1940, 1196). Furthermore, the mechanism used to explain the formation of 1 : 2 : 5 : 6-tetramethylnaphthalene and 1 : 5 : 6-trimethyl-β-naphthol from α-amyrin (Spring and Vickerstaff, J., 1937, 249; Brunner, Hofer, and Stein, *Monatsh.*, 1932, **61**, 293; 1933, **63**, 79) would not be valid.

A method of testing the partial formula (I) for α-amyrin is apparently afforded by α-amyrenonol, which will be represented by (III); under suitable reaction conditions, dehydration of α-amyrenonol would be expected to give an α-amyradienone (IV) containing a conjugated diene-one chromophore. Spring and Vickerstaff (*loc. cit.*) showed that dehydration of α-amyrenonol with phosphorus pentachloride gives a mixture of the two

unsaturated ketones, α-amyradienone-I and α-amyradienone-II. We have examined the absorption spectra of these isomers; both exhibit maxima in the neighbourhood of 2500 A. ($\varepsilon_{max.} \simeq 12{,}000$) closely approximating to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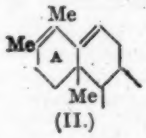
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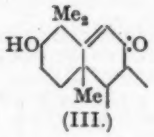
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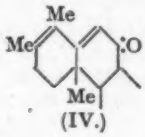
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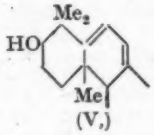
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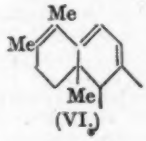
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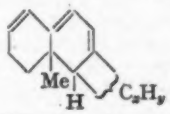

(VII*a*) $x = 16, y = 30$
(VII*b*) $x = 17, y = 30$

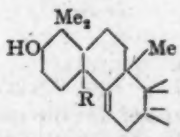
that of α-amyrenonol, thus showing that dehydration of the latter by means of phosphorus pentachloride has not led to an increase in conjugation. Dehydration of α-amyrenonol with phosphoric oxide gives a mixture of α-amyradienone-II and an amorphous phosphorus-containing substance; the reagent which converts α-amyrin into the conjugated *l*-α-amyradiene has not led to an increase in conjugation in the case of α-amyrenonol.

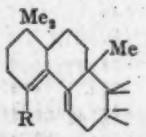
Treatment of α-amyrenonol with hydriodic acid–acetic acid mixture gives an *α-amyradienone*-III, m. p. 169°, which exhibits two absorption bands situated at 2600 A. ($\varepsilon_{max.} = 12{,}000$) and 2920 A. ($\varepsilon_{max.} = 11{,}000$). Although the intensity and location of these well-defined maxima are not modified by repeated crystallisation of the unsaturated ketone, we have not overlooked the possibility that the compound, m. p. 169°, may be a mixed crystal of the true α-amyradienone-III containing the chromophoric system in (IV) together with an isomer containing an isolated ethylenic linkage and an αβ-unsaturated keto-group. The former component would give rise to the absorption maximum at 2920 A. (Picard and Spring, J., 1941, 35) and the latter to the maximum in the neighbourhood of 2600 A. However, α-amyradienone-III could not be resolved by the chromatographic method using activated alumina. It is of interest that, when treated with hydriodic acid–acetic acid mixture, α-amyrin yields *l*-α-amyradiene.

Attention was next directed to the dehydration of α-amyradienol, which we have previously shown contains a conjugated system of ethylenic linkages in one ring (Spring and Vickerstaff, *loc. cit.*; Ewen, Spring, and Vickerstaff, J., 1939, 1303). If the partial formulæ (I) and (III) be assumed for α-amyrin and α-amyrenonol respectively, α-amyradienol will be (V). Treatment of the dienol with phosphorus pentachloride gives *dichloro-α-amyradiene*, m. p. 128—129°, which exhibits a maximum at 2800 A. ($\varepsilon_{max.} = 11{,}800$). Treatment of dichloro-α-amyradiene with zinc dust and acetic acid gives *d-α-amyratriene*, m. p. 131—133°, $[\alpha]_D + 439°$, exhibiting an absorption maximum at 2810 A. ($\varepsilon_{max.} = 11{,}000$). The absorption spectra of α-amyradienyl acetate (max. 2800 A., $\varepsilon_{max.} = 11{,}500$), dichloro-α-amyradiene, and *d*-α-amyratriene are strikingly similar both in location of the maxima and in intensity of absorption, showing that the dehydration of α-amyradienol (to give *d*-α-amyratriene) has not led to an increase in conjugation, the introduced ethylenic linkage being isolated from the diene chromophore.

Dehydration of α-amyradienol with phosphoric oxide gives *l-α-amyratriene*, m. p. 140—142°, $[\alpha]_D - 450°$, which exhibits an absorption maximum at 2950 A. ($\varepsilon_{max.} = 33{,}000$). The absorption spectrum of this hydrocarbon establishes that its three ethylenic linkages are conjugated; in terms of the α-amyrin partial formula (I) the simplest representation of *l*-α-amyratriene is (VI). Neither *l*-α-amyradiene nor *l*-α-amyratriene reacts with maleic anhydride in boiling benzene solution. However, it is not possible, as yet, to define more closely the environment of the conjugated triene system in *l*-α-amyratriene. Although the ergostatetraene described by Windaus and Buchholz (*Ber.*, 1939, **72**, 598), which probably contains a conjugated triene system, exhibits a maximum at approximately 2900 A. ($\varepsilon_{max.} = 35{,}000$) in very close agreement with that of *l*-α-amyratriene, and the cholestatriene formulated as (VII*a*) exhibits a maximum at 3020 A. (Eckhardt, *Ber.*, 1938, **71**, 461), dehydroergosterol, dehydrolumisterol (Heilbron, Moffet, and Spring, J., 1937, 413), and the ergostatetraene formulated as (VII*b*) (Heilbron, Kennedy, Spring, and Swain, J., 1938, 869) all exhibit maxima in the neighbourhood of 3200. The reason for this variation is almost certainly to be found in differences in the molecular environment of the triene system; formulations such as (VII) for cholestatriene and ergostatetraene are not rigidly established.

(VIII.)




(IX.)

The dehydration of α-amyrin and α-amyradienol to *l*-α-amyradiene and *l*-α-amyratriene, respectively, establishes a relatively close association of the hydroxyl and the ethylene linkage in the α-amyrin group of triterpenes. However, it is not established that the ethylenic linkage is situated between $C_6$ and $C_7$, an alternative partial formulation for α-amyrin and *l*-α-amyradiene being shown at (VIII) and (IX) respectively. It is

hoped that a further examination of the degradation products described in this paper, and in particular of *l*-α-amyradiene, will define more closely the position of the unsaturated centre in the α-amyrin series.

## Experimental.

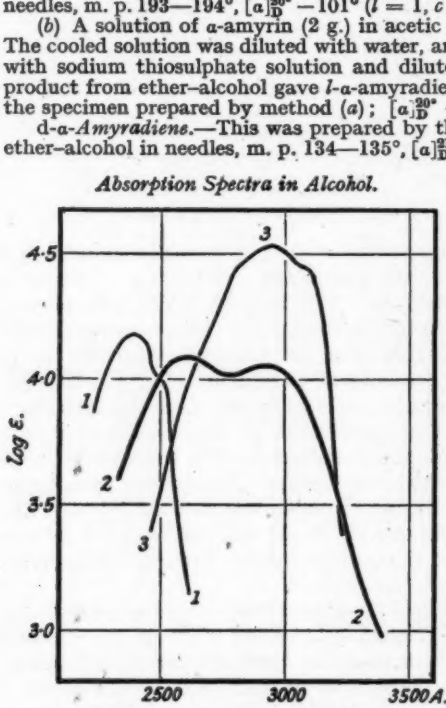
Specific rotations were measured in chloroform solution; m. p.'s are uncorrected.

α-*Amyradiene.*—(*a*) The hydrocarbon prepared as described by Vesterberg (*loc. cit.*) was obtained in prismatic needles, m. p. 193—194°, $[\alpha]_D^{20°}$ −101° (*l* = 1, *c* = 0·8). It gave a brown coloration with tetranitromethane in chloroform.

(*b*) A solution of α-amyrin (2 g.) in acetic acid (20 c.c.) was refluxed with hydriodic acid (*d* 1·7; 8 c.c.) for 4 hours. The cooled solution was diluted with water, and the mixture extracted with ether; the extract was washed successively with sodium thiosulphate solution and dilute hydrochloric acid. Removal of the solvent and crystallisation of the product from ether–alcohol gave *l*-α-amyradiene in prismatic needles, m. p. 193—194° either alone or when mixed with the specimen prepared by method (*a*); $[\alpha]_D^{20°}$ − 104° (*l* = 1, *c* = 1·5).

d-α-*Amyradiene.*—This was prepared by the method of Vesterberg and Westerlind (*loc. cit.*); it was obtained from ether–alcohol in needles, m. p. 134—135°, $[\alpha]_D^{21°}$ + 109° (*l* = 0·5, *c* = 0·7 in chloroform). *d*-α-Amyradiene was recovered unchanged after shaking with phosphoric oxide in benzene solution for 48 hours. α-Amyradienone-I was obtained by the method of Spring and Vickerstaff (*loc. cit.*); it separates from alcohol in needles, m. p. 197°. *Light absorption in alcohol:* Maximum at 2490 A., ε = 14,000.

*Absorption Spectra in Alcohol.*




1. l-α-*Amyradiene.* 2. α-*Amyradienone*-III. 3. l-α-*Amyratriene.*

α-*Amyradienone*-II.—A solution of α-amyrenonol (5 g.) in ether (30 c.c.) was shaken for 24 hours with phosphoric oxide (2 g.). The solution was washed with water and dried (sodium sulphate), and the residue obtained after removal of the solvent extracted with hot acetone. The insoluble fraction separated from ethyl acetate as an amorphous powder, m. p. 205—209°. This substance contained phosphorus which could not be removed either by attempted crystallisation or by filtration through a column of alumina. Repeated crystallisation of the acetone-soluble fraction from alcohol gave α-amyradienone-II in needles, m. p. 162—163°. When prepared by the dehydration of α-amyrenonol with phosphorus pentachloride, α-amyradienone-II was obtained in needles, m. p. 160—161°, undepressed by the specimen described above. It gave a yellow coloration with tetranitromethane (Found: C, 85·4; H, 11·1. Calc. for $C_{30}H_{46}O$: C, 85·25; H, 11·0%). *Light absorption in alcohol:* Maximum at 2520 A., ε = 13,000.

α-*Amyradienone*-III.—A mixture of α-amyrenonol (5 g.), glacial acetic acid (50 c.c.), and hydriodic acid (*d* 1·7; 15 c.c.) was refluxed for 8 hours. The cold solution was diluted with water and extracted with ether; the extract was washed with sodium thiosulphate, dilute hydrochloric acid, and water. Removal of the ether and repeated crystallisation of the residue from methyl alcohol gave α-*amyradienone*-III as laminæ, m. p. 179°, $[\alpha]_D^{20°}$ + 170° (*l* = 1, *c* = 2·3 in chloroform). It gave a yellow coloration with tetranitromethane in chloroform (Found: C, 85·2; H, 10·9. $C_{30}H_{46}O$ requires C, 85·25; H, 11·0%).

α-*Dichloroamyradiene.*—α-Amyradienol (Ewen, Spring, and Vickerstaff, *loc. cit.*) (m. p. 159—160°; 1·9 g.) in light petroleum (b. p. 60—80°; 50 c.c.) was shaken with phosphorus pentachloride (0·93 g.). When the evolution of hydrogen chloride had diminished (1 hour) the mixture was heated under reflux for 2 minutes, cooled, and washed with warm water. Removal of the solvent from the dried (sodium sulphate) solution and three crystallisations of the residue from alcohol gave α-*dichloroamyradiene* in needles, m. p. 128—129°, $[\alpha]_D^{21°}$ +407° (*l* = 0·5, *c* = 0·5 in chloroform) (Found: C, 75·4; H, 9·4. $C_{30}H_{46}Cl_2$ requires C, 75·4; H, 9·7%).

d-α-*Amyratriene.*—A solution of α-dichloroamyradiene (0·5 g.) in acetic acid (5 c.c.) was heated, under reflux, with zinc dust (0·2 g.) for 4 hours. The hot liquid was filtered and diluted with water. The solid separating was collected, washed with water, and dried. Two crystallisations from absolute alcohol gave d-α-*amyratriene* in long silky needles, m. p. 131—133°, $[\alpha]_D$ +439° (*l* = 1, *c* = 1·6) (Found: C, 88·4; H, 11·5. $C_{30}H_{46}$ requires C, 88·6; H, 11·4%). *d*-α-Amyratriene gave an intense brown coloration with tetranitromethane in chloroform.

l-α-*Amyratriene.*—A solution of α-amyradienol (1 g.) in dry benzene (30 c.c.) was shaken for 24 hours with phosphoric oxide (1·5 g.). The mixture was washed with warm water, and the filtered solution evaporated to dryness. Four crystallisations of the residue from alcohol gave l-α-*amyratriene* in needles, m. p. 140—142°. The hydrocarbon gave a red-brown coloration with tetranitromethane in chloroform, which was considerably more intense than that produced by α-amyradienol, $[\alpha]_D^{20°}$ − 450° (*l* = 1, *c* = 0·8] (Found: C, 88·6; H, 11·7. $C_{30}H_{44}$ requires C, 88·6; H, 11·4%).

We thank the Carnegie Trust for the award of a scholarship which enabled one of us (E. S. E.) to participate in this work.

The University, Manchester. [*Received, October 26th,* 1943.]

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## 16. *The Constitution of Yeast Ribonucleic Acid. Part VII. Diffusion Coefficients and Molecular Weights.*

By W. E. Fletcher, J. Masson Gulland, D. O. Jordan, and in (part) H. E. Dibben.

From measurements of diffusion coefficients it is concluded that yeast ribonucleic acids of different origin have molecular weights ranging between those corresponding to 8 and 18 hypothetical tetranucleotides. Deamination of B.D.H. yeast ribonucleic acid under special conditions does not diminish the molecular weight, confirming the conclusion already reached that phospho-amide groups do not play an essential part in linking nucleotides in the acid from that source. Less controlled conditions cause extensive molecular degradation.

THE values of the molecular weight of yeast ribonucleic acid previously recorded show considerable disagreement. Myrbäck and Jorpes (*Z. physiol. Chem.*, 1935, **237**, 159), using the method of free diffusion described by Ohölm (*Z. physikal. Chem.*, 1904, **50**, 309), determined the molecular weight of a sample of yeast ribonucleic acid prepared by Merck, and obtained values between 1300 and 2150 in the presence of 5% sodium chloride. Loring (*J. Biol. Chem.*, 1939, **128**, Sci. Proc., **33**, 61), using the method of Northrop and Anson (*J. Gen. Physiol.*, 1928—29, **12**, 543), obtained values for the diffusion coefficient of 0·13—0·11 cm.² per day, giving values for the molecular weight of 17,000—28,000. Fischer, Böttger, and Lehmann-Echternacht (*Z. physiol. Chem.*, 1941, **271**, 246), using Jander and Spandau's (*Z. physikal. Chem., A*, 1939, **185**, 325; 1940, **187**, 13) modification of Brintzinger's dialysis method (see *ibid.*, p. 317), obtained a value of 10,300 for the molecular weight of Boehringer yeast ribonucleic acid. Bredereck and Hoepfner (*Ber.*, 1942, **75**, 1086), using the same method, give the value of 1177 for the product isolated after the mild alkaline hydrolysis of yeast ribonucleic acid. This material they consider to be the fundamental tetranucleotide unit.

In Table I are given the diffusion coefficients ($D$) at 25° for various samples of yeast ribonucleic acid in N-sodium sulphate, calculated by using Mehl and Schmidt's equation (*Univ. Cal. Pub. Physiol.*, 1937, **8**, 165). The constancy of the values with decreasing concentration of the nucleic acid indicates the absence of abnormal diffusion processes.

TABLE I.

| Sample of yeast nucleic acid. | Cell. | Nucleic acid concn., %. | Buffer. | Time, hrs. | $D$, cm.²/day. |
|---|---|---|---|---|---|
| B.D.H. Y21 | 1 | 0·66 | Borate pH 8·0 | 1 | 0·116 |
| | 1 | 0·97 | ,, | 1 | 0·114 |
| | 1 | 1·20 | ,, | 1 | 0·116 |
| | 4 | 0·97 | ,, | 5 | 0·115 |
| | 4 | 0·97 | ,, | 24 | 0·116 |
| | 4 | 1·90 | ,, | 43·5 | 0·117 |
| B.D.H. Y8 | 4 | 1·53 | Acetate pH 5·8 | 17 | 0·105 |
| | 4 | 1·53 | ,, | 23 | 0·106 |
| | 4 | 1·53 | ,, | 26 | 0·105 |
| | 1a | 1·04 | (None) pH 7·0 | 4·5 | 0·099 |
| | 1a | 0·62 | ,, | 3 | 0·102 |
| Boehringer BY1 | 1 | 1·40 | Borate pH 8·0 * | 1 | 0·139 |
| | 1 | 0·63 | ,, | 1 | 0·124 |
| | 1 | 0·11 | ,, | 2 | 0·138 |
| Eastman Y9 | 1a | 0·71 | (None) pH 6·9 | 16 | 0·105 |
| | 1a | 0·71 | ,, | 5 | 0·102 |
| | 1a | 0·71 | ,, | 17 | 0·100 |
| Merck Y10 | 4 | 0·76 | (None) pH 7·0 | 22 | 0·104 |
| | 4 | 0·76 | ,, | 23 | 0·107 |
| | 4 | 0·76 | ,, | 29·5 | 0·115 |
| Product of mild alkaline hydrolysis | 1 | 0·80 | Borate pH 8·0 | 1 | 0·162 |
| Deaminated B.D.H. DY33 ..... | 1 | 0·80 | ,, | 1 | 0·114 |
| DY5 ..... | 4 | 1·33 | Acetate pH 5·8 | 22 | 0·105 |
| | 4 | 1·33 | ,, | 23 | 0·096 |
| | 4 | 1·33 | ,, | 47·5 | 0·102 |
| Boiled sample of DY5 | 4 | 0·44 | (None) pH 7·0 | 19 | 0·227 |
| | 4 | 0·44 | ,, | 22·5 | 0·242 |
| | 4 | 0·44 | ,, | 22·5 | 0·256 |

* N-Sodium chloride in place of N-sodium sulphate.

By application of the Stokes–Einstein equation to the values of the diffusion coefficient, a value of the molecular radius may be obtained on the assumption that the diffusing ion is spherical—an assumption which is justifiable provided that the asymmetry of the molecule be not too great. The molecular weight may then be directly obtained from this value of the molecular radius and the specific weight of the diffusing particle. In Table II the approximate values of the molecular weights determined from the mean diffusion coefficients are given. The value of the specific weight of yeast ribonucleic acid and of deaminated yeast ribonucleic acid was taken as 1·70 g. per c.c.

TABLE II.

| Sample of yeast ribonucleic acid. | $D$, cm.²/day. | $M$. | Sample of yeast ribonucleic acid. | $D$, cm.²/day. | $M$. |
|---|---|---|---|---|---|
| B.D.H. Y21 ..... | 0·116 [3] | 15,830 | Product of mild alkaline hydrolysis [1] ..... | 0·162 [5] | 5,810 |
| Y8 ..... | 0·102 [6] | 22,550 | Deaminated B.D.H. DY33 [2] ... | 0·114 [5] | 16,690 |
| Boehringer BY1 ..... | 0·134 [5] | 10,280 | DY5 [3] ..... | 0·102 [6] | 22,550 |
| Eastman Y9 ..... | 0·102 [5] | 23,250 | Boiled sample of DY5 [4] ..... | 0·242 [7] | 1,830 |
| Merck Y10 ..... | 0·108 [5] | 19,630 | | | |

[1] Prepared according to the method of Bredereck and Hoepfner (*loc. cit.*). [2] Prepared from B.D.H. Y21.
[3] Prepared from B.D.H. Y8. [4] Contained a trace of inorganic phosphorus. [5] Borate buffer at pH 8·0.
[6] Acetate buffer at pH 5·8. [7] Unbuffered N-$Na_2SO_4$ solution at pH 7·0.

It is to be concluded from the data in Table II that the preparations of yeast ribonucleic acid investigated are polynucleotides, built up of 8—18 tetranucleotide units, although it must be emphasised that there is as

yet little evidence for the existence of the tetranucleotide as a chemical entity. The isolation of a product having a molecular weight of 5810 in place of the product of molecular weight 1177 obtained by Bredereck and Hoepfner (*loc. cit.*), after the mild alkaline hydrolysis of Boehringer yeast ribonucleic acid, suggests that the nature of the hydrolysis product is very dependent on the conditions of hydrolysis, and possibly also on the molecular size of the starting material.

The diffusion coefficients and molecular weights of deaminated B.D.H. yeast ribonucleic acid are of the same order (Table II) as those of the original acid. This may be interpreted as indicating that both these substances are similarly constituted; and that a P–N linkage involving a primary amino-group is not an essential structure in the polynucleotide, thus confirming the conclusions of Falconer, Gulland, Hobday, and Jackson (J., 1939, 907).

## Experimental.

*Determination of the Diffusion Coefficient.*—The diffusion coefficient of molecules possessing high molecular weight may be determined by the porous disc method of Northrop and Anson (*loc. cit.*), who in applying Fick's law ($dQ/dt = Ddc/dx$, where $dQ$ is the amount of substance diffusing across an area of 1 cm.$^2$ in time $dt$ under a concentration gradient $dc/dx$) assume that $dc/dx = (c' - c'')/h$, where $c'$ and $c''$ are the concentrations on either side of the porous disc in the diffusion cell, and $h$ is the effective thickness of the porous disc. This assumption introduces the restriction that the variation of $c'$ and $c''$ during the experiment must be small; Northrop and Anson suggest that the maximum permissible variation in $c'$ is 3%. McBain and Liu (*J. Amer. Chem. Soc.*, 1931, **53**, 59), using the same experimental method, assume that the variation of the concentration within the cell over a considerable time period is negligible. The technique of the method has been improved by Mehl and Schmidt (*loc. cit.*), who, by changing the outer solution of the diffusion cell at increasingly frequent intervals during a preliminary period when the diffusion gradient is being established, commence the measured diffusion period with the concentration of the solution at the lower surface of the porous disc very nearly zero. To determine the diffusion coefficient, Mehl and Schmidt use the following equation, which is derived from Fick's law by integration over the time interval $t$ and is therefore valid for any value of $t$ irrespective of the magnitude of the change in concentration:

$$D'kt = [V''V'/(V'' + V')]\{\ln c_0'' - \ln [c_0'' - (1 + V'/V'')c']\}$$

where $D'$ is the integral diffusion coefficient representing a mean value over a range of concentration, $k$ the cell constant, and $t$ the time interval; $V''$ is the volume and $c_0''$ the original concentration of the upper solution, $V'$ is the volume of the lower solution and $c'$ the concentration after diffusion over the time period $t$.

During the diffusion of ions of high molecular weight, an electrical potential may be established by the rapid diffusion of the more mobile ions of opposite charge. It is therefore necessary (see, *e.g.*, Hartley and Robinson, *Proc. Roy. Soc., A*, 1931, **134**, 20; Valko, *Trans. Faraday Soc.*, 1935, **31**, 230), in order to obtain a value for the diffusion coefficient which may be used in the Stokes–Einstein equation for the evaluation of the particle radius, to carry out the determination of the diffusion coefficient in the presence of a considerable excess of electrolyte.

*Apparatus.*—The diffusion cells used were similar to those described by Northrop and Anson (*loc. cit.*). The porous diaphragms were sintered glass discs, porosity number 4, and had the following dimensions: cell 1 and 1a, 50 mm. in diam., 0·5 mm. thick; cell 4, 30 mm. in diam., 2 mm. thick. In order to prevent evaporation of the lower solution, a rubber ring was fitted between the cell and the outer vessel as described by McBain and Liu (*loc. cit.*). To reduce vibration to a minimum, the cells were mounted on a slate bench built into a main structural wall. The air temperature was maintained at 25° ± 0·2°.

The cell constant was determined by using 2N-sodium chloride as the diffusing solution. The diffusion constant of sodium chloride at this concentration has been given by Anson and Northrop (*J. Gen. Physiol.*, 1937, **20**, 575) as 1·26 cm.$^2$/day. This solution has the advantage that the diffusion coefficient remains constant when the concentration is decreased. The method of manipulation was carried out as described by Mehl and Schmidt (*loc. cit.*). The outer solution was analysed for chloride by titration with 0·1N-silver nitrate. The values for the cell constants were: cell 1, 30·0; cell 1a, 30·5; cell 4, 2·62.

The diffusion of yeast ribonucleic acid was carried out in Clark and Lubs' borate buffer, pH 8, and in acetate buffer, pH 5·8, containing added electrolyte; and also in unbuffered N-sodium sulphate solution. The nucleic acid concentration in the outer solution was determined by estimating the phosphorus content by Briggs' modification (*J. Biol. Chem.*, 1922, **53**, 13) of Bell and Doisy's colorimetric method (*ibid.*, 1930, **44**, 55). The nucleic acid before dissolution was dried in a vacuum over phosphoric oxide at 100° to constant weight, and analysed by the same method and by the strychnine phosphomolybdate method [Embden, *Z. physiol. Chem.*, 1920, **113**, 138, modified by Still (unpublished)] which gave identical results.

The determination of the specific weight of the samples of nucleic acid was carried out by two methods. (1) The specific weight of the solid nucleic acid was determined by the usual method using a specific gravity bottle (10 c.c.) and pure, dry benzene as the inert liquid. (2) The specific volume of the nucleic acid ion was determined pycnometrically and calculated from the formula $v_2 = [n_0 - (n_1 - n_2)]/d_0 n_2$, where $v_2$ is the specific volume of the nucleic acid ion, $n_0$ and $n_1$ are the weights of solvent and solution respectively contained in the pycnometer, $n_2$ is the weight of solute present in $n_1$ g. of solution, and $d_0$ is the density of the solvent. The specific weight is the reciprocal of the specific volume. The values obtained by the two methods were in agreement, although variations from 1·65 to 1·80 g. per c.c. were obtained. These variations may be attributed to the hygroscopic nature of nucleic acid which introduces an inaccuracy during weighing.

The measurement of the viscosity of the nucleic acid solutions, required in the Stokes–Einstein equation, was determined at 25° by means of an Ostwald viscometer.

*Purification of Yeast Ribonucleic Acid.*—The samples of this acid were supplied by B.D.H., Boehringer, Merck, and Eastman. The commercial samples were purified by a method similar to that described by Makino (*Z. physiol. Chem.*, 1935, **236**, 206). Yeast ribonucleic acid (60 g.) was suspended in cold water (1650 c.c.) and dissolved by the addition of 2N-ammonium hydroxide (80 c.c.) with mechanical stirring. This solution had pH *ca.* 5·8. After being filtered, it was poured with vigorous stirring into alcohol (3460 c.c.) containing concentrated hydrochloric acid (20 c.c.). The final pH of this solution was 2·2. The white gelatinous precipitate of nucleic acid was collected, stirred with 66% alcohol (500 c.c.), and again collected. The nucleic acid was resuspended in cold water (1000 c.c.) and dissolved by the slow addition of 2N-ammonium hydroxide (65 c.c.). The resulting solution was filtered and poured slowly into alcohol (2130 c.c.) containing concentrated hydrochloric acid (17 c.c.); the final solution had pH 2·0. The precipitated nucleic acid was collected, repeatedly washed by being vigorously dispersed in 66% alcohol until free from chloride ions, and finally collected and washed successively with 80% alcohol, 100% alcohol, and ether, and dried in a vacuum over phosphoric oxide and potassium hydroxide. The yield was 40 g. (Found, in samples dried at 110° in a vacuum over phosphoric oxide: B.D.H., Y1: N, 16·2; P, 8·8. Y2: N, 16·0; P, 8·6. Y21: N, 16·0; P, 8·8. Y8: N, 16·3; P, 8·9. Boehringer, BY1: N, 15·8;

P, 9·1. Merck, Y10: N, 16·1; P, 9·3. Eastman, Y9; N, 15·7; P, 8·9. Calc., for a tetranucleotide containing 1 mol. of the nucleotides, adenylic, guanylic, uridylic, and cytidylic acids, $C_{38}H_{47}O_{28}N_{15}P_4$: N, 16·3; P, 9·5%).

A specimen of nucleic acid having a lower molecular weight was prepared by the mild alkaline hydrolysis of purified Boehringer yeast ribonucleic acid, as described by Bredereck and Hoepfner (*loc. cit.*) (Found, in sample dried at 110° in a vacuum: N, 15·6; P, 8·8%).

*Deamination of Yeast Ribonucleic Acid* (with H. E. Dibben).—A method of deaminating yeast ribonucleic acid has been described by Bredereck, Köthnig, and Lehmann (*Ber.*, 1938, **71**, 2613) in which the acid, in neutral solution, was treated with sodium nitrite and acetic acid at room temperature, and the deaminated nucleic acid subsequently precipitated as the lead salt. This was suspended in water and decomposed by hydrogen sulphide; these authors do not record the temperature at which this process was carried out, but we have found that the lead sulphide is coagulated satisfactorily only when the treatment is in hot water; cold decomposition of the salt proved quite unsuccessful. The filtrate from lead sulphide was then concentrated to small volume under reduced pressure, and the deaminated nucleic acid precipitated by the addition of alcohol, collected, and dried.

The electrometric titration (Part VIII; following paper) of samples of deaminated acid, prepared as described by Bredereck, Köthnig, and Lehmann and including heat decomposition of the lead salt, suggested that the number of acidic groups of the product was dependent on the length of time for which the solution was heated during the precipitation of the lead sulphide.

We therefore consider the method of Bredereck *et al.* to be unsatisfactory, owing to the difficulty of removing the last traces of sodium acetate and the probability of decomposition occurring during the treatment with hydrogen sulphide. An attempt was therefore made to bring about deamination by using amyl nitrite in acetic acid solution at room temperature and at 40° for various lengths of time, followed by alcohol precipitation. Determination of the amino-nitrogen by the van Slyke method, however, showed that the maximum deamination obtained was only 10% of the theoretical.

The following method was finally adopted for the deamination of yeast ribonucleic acid; precipitation as the lead salt can be avoided if potassium salts are used, because potassium acetate is sufficiently soluble in alcohol to escape precipitation along with the deaminated acid. Purified acid (10 g.) was suspended in water (20 c.c.) and dissolved by adding slowly 0·5N-potassium hydroxide (44 c.c.); the pH of the solution remained below 6·0 throughout this operation. The solution was transferred to a narrow-necked flask, and potassium nitrite (20 g.) dissolved in water (10 c.c.) added, together with a few drops of capryl alcohol to prevent frothing. The flask was closed by a Bunsen valve, and glacial acetic acid added slowly over a period of 2 hours. The mixture stood at room temperature for 48 hours; nitrous acid was then still present. The solution was then poured into alcohol (150 c.c.) containing concentrated hydrochloric acid (6 c.c.). The precipitated deaminated ribonucleic acid was collected, washed with 66% alcohol, suspended by stirring in cold water (30 c.c.), and dissolved by slowly adding 2N-ammonium hydroxide (12 c.c.); the solution had a pH value of 5·0. The deaminated acid was then finally precipitated by pouring this solution into alcohol (78 c.c.) containing concentrated hydrochloric acid (4 c.c.); the final pH of this solution was 1·6. The precipitate was collected, washed with 75% alcohol until free from chloride, nitrite, and nitrate ions, then with 80% alcohol, 100% alcohol, and ether, and dried in a vacuum over phosphoric oxide and potassium hydroxide. The yield was 4 g. (Found, in samples dried at 110° over phosphoric oxide in a vacuum; DY33: N, 13·3; P, 8·9. DY 5: N, 13·1; P, 8·9. Calc. for deaminated tetranucleotide containing 1 mol. of each of the nucleotides inosinic and xanthylic acids and 2 mols. of the nucleotide uridylic acid, $C_{38}H_{44}O_{31}N_{12}P_4$: N, 12·9; P, 9·5%).

Deaminated yeast ribonucleic acid undergoes hydrolysis when an aqueous solution of the acid is heated; it has been shown by electrometric titration (see Part VIII) that this hydrolysis is complete after heating at 100° for 10 minutes. The isolation of the hydrolysis product was attempted by concentrating the solution under reduced pressure and precipitating it by addition of alcohol containing hydrochloric acid. The product was contaminated by free purines; for this reason the determination of the diffusion coefficient of the hydrolysis product was carried out on the solution obtained after hydrolysis, which contained only a trace of free purine.

The microanalyses were carried out by Mr. J. E. Still. It is a pleasure to record the help given by Imperial Chemical Industries Ltd. in the form of grants for chemicals and apparatus.

University College, Nottingham. [*Received, November 19th*, 1943.]

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## 17. *The Constitution of Yeast Ribonucleic Acid. Part VIII. Electrometric Titration of the Acid Groups.*

By W. E. Fletcher, J. Masson Gulland, and D. O. Jordan.

The titration of the acidic groups of samples of yeast ribonucleic acid has been performed electrometrically, hydrogen and glass electrodes being used. Yeast ribonucleic acid is found to possess four acid dissociations per tetranucleotide when existing as a polytetranucleotide, three of which are primary dissociations, and one a secondary dissociation of phosphoric acid. The deaminated acid is found to be similarly constituted. Mild hydrolysis reduces the molecular weight of the polytetranucleotide, and the titration results suggest that a further secondary dissociation of phosphoric acid is liberated. The formulæ which have been proposed previously for yeast ribonucleic acid are not in agreement with these data, and a modified formula is proposed; this is discussed in relation to the existing molecular weight and enzyme data.

The titration of the acid groups of yeast ribonucleic acid has been carried out previously by two methods: electrometrically, by Levene and Simms (*J. Biol. Chem.*, 1926, **70**, 327), Jorpes (*Biochem. J.*, 1934, **28**, 2102), and Allen and Eiler (*J. Biol. Chem.*, 1941, **137**, 757); and by titrating with alkali to the phenolphthalein end-point, thus titrating both the primary and the secondary phosphoric acid dissociation, by Makino (*Z. physiol. Chem.*, 1935, **232**, 229), Bredereck and Köthnig (*Ber.*, 1939, **72**, 121), and Bredereck and Jochman (*ibid.*, 1942, **75**, 395).

Levene and Simms titrated two different samples of yeast ribonucleic acid, and found 4·5 and 3·0 acid dissociations per tetranucleotide respectively at pH 8 (at this point the titration of primary and secondary dissociating groups of phosphoric acid is complete). The considerable discrepancy between their experimental

results and the theoretical curve constructed on the supposition that four primary and one secondary acid dissociations were present was accounted for by suggesting the formation of anhydrides, but this explanation was not further elaborated. The results obtained by Jorpes cannot be fully interpreted, since, for the purpose of comparing the titration curves of various mixtures of nucleic acid and nucleotides, a water-soluble salt of ribonucleic acid was titrated to pH 2 with an unknown quantity of acid prior to the titration with alkali. Allen and Eiler, using an Eastman preparation of yeast ribonucleic acid, found four acid dissociations per tetranucleotide at pH 8 after correcting for the presence of a small quantity of sodium salt present in the nucleic acid preparation.

Makino, using Merck's yeast ribonucleic acid, found that 2·86 acid dissociations were titrated at the phenolphthalein end-point (pH 8); this low figure was attributed to the presence of sodium nucleate, and on correcting for that part of the acid already neutralised, Makino obtained 3·73 acid dissociations per tetranucleotide. The sample on analysis showed a low phosphorus content, and Makino concluded that the acid was tetrabasic. On alkaline hydrolysis an additional 3·93 acid dissociations per tetranucleotide were obtained. Similar results were obtained for Boehringer and Takida preparations of yeast ribonucleic acid. Bredereck and his collaborators, who had found that consistent results could be obtained by titrating the desoxyribonucleic acid of thymus, observed that inconsistent results were obtained with yeast ribonucleic acid; but they concluded that most probably there were four acidic dissociations per tetranucleotide.

The titration of the acid groups of deaminated yeast ribonucleic acid to the phenolphthalein end-point has been attempted by Bredereck, Köthnig, and Lehmann (*Ber.*, 1938, **71**, 2613), who considered the impure product to be tetrabasic, but suggested that further purification might cause an increase in the number of acid dissociations. Bredereck and Hoepfner (*Ber.*, 1942, **75**, 1086) have recently prepared a material believed by them to be a deaminated tetranucleotide, which by titrating to the phenolphthalein end-point they found to be pentabasic, with the liberation of a further three acid dissociations on alkaline hydrolysis.

*Results of the Present Investigation.*—It will be convenient to follow other workers and calculate the results in terms of acid dissociations per tetranucleotide, assuming that this contains one of each of the nucleotides guanylic, adenylic, cytidylic, and uridylic acids.

The titration curve of yeast ribonucleic acid is given in Fig. 1, curves I and II. Curve I has been obtained for four different samples of purified B.D.H. yeast ribonucleic acid (Y1, Y2, Y21, Y8). Several separate titrations have been carried out on the sample Y1, and the results found to be accurately reproducible. A point of inflection is obtained at pH 8 which corresponds to the neutralisation of 3·4 acid dissociations per tetranucleotide. A similar curve (Fig. 1, curve II) was obtained for a purified sample of Boehringer yeast ribonucleic acid (BY1), a point of inflection occurring at pH 8 after the neutralisation of 3·6 acid dissociations per tetranucleotide. A second point of inflection has been obtained for all these preparations at pH 11·5 after the addition of a further 2·2 equivs. of alkali. The dissociating groups titrated in this pH range are most probably the hydroxyl groups of uracil and guanine in the 6-position, which are titrated over this range (Levene and Simms, *J. Biol. Chem.*, 1925, **65**, 519; 1926, **70**, 327; confirmed by us). The additional 0·2 equiv. in excess of the theoretical is to be attributed to a small amount of hydrolysis occurring in the alkaline solution. This suggestion is confirmed by the data obtained on back-titrating with acid from pH 12 immediately after titrating with alkali; an increase of 0·4 equiv. was obtained at pH 8. Very similar titration curves have been obtained for Merck (Y10, curve III) and Eastman (Y9, curve IV) preparations of yeast ribonucleic acid.

Samples of B.D.H. yeast ribonucleic acid (Y1) were hydrolysed at room temperature by standing in excess alkali (pH 12·5) and back-titrating with acid. The results of the back-titration are given in curve V, a similar curve being obtained after 22 days' and 38 days' hydrolysis. A point of inflection occurs at pH 8 corresponding to the neutralisation of 7·4 acid dissociations per tetranucleotide, an increase of 4 over the unhydrolysed substance. A second point of inflection may be discerned at pH 5, corresponding to the neutralisation of 3·6 acid dissociations. Similar results were obtained with the sample of Boehringer yeast ribonucleic acid (curve VI), which was hydrolysed by standing for 13 days at pH 11·8 at room temperature. Less alkali was used in this hydrolysis to increase the accuracy of the back titration. The cold alkaline hydrolysis (Levene, *J. Biol. Chem.*, 1923, **55**, 9; Jones and Perkins, *ibid.*, p. 567; 1924, **62**, 557; Calvery and Jones, *ibid.*, 1927, **73**, 73; Buell and Perkins, *ibid.*, 1927, **72**, 21; Calvery and Remson, *ibid.*, 1927, **73**, 593) transforms the yeast ribonucleic acid into nucleotides; provided that this hydrolysis were complete, four acid dissociations would be liberated per tetranucleotide if one acid group per nucleotide took part in the internucleotide linkage in the polynucleotide. This explanation is in agreement with the above data.

Bredereck and Hoepfner (*loc. cit.*) have described the preparation, by the mild alkaline hydrolysis of Boehringer yeast ribonucleic acid, of a substance which they consider to be a tetranucleotide. Their preparation has been repeated upon purified Boehringer yeast ribonucleic acid (BY2), and a sample of lower molecular weight isolated (BY21) (see Part VII, preceding paper). The titration of the original acid used for this preparation is given in curve VII, and that of the product of the mild hydrolysis in curve VIII; at pH 8, 4·5 acid dissociations have been titrated, an increase of 0·6 over the original acid. After hydrolysis of the Boehringer acid (BY2) in strong alkali at pH 12, as described above, curve IX was obtained on back titration with acid: it is in close agreement with curve VI, obtained with another sample of Boehringer yeast nucleic acid (BY1).

The results of the titration of deaminated yeast ribonucleic acid are given in Fig. 2, curve X, which has been obtained on several occasions (DY1, DY33, DY5). The titration curve exhibits three well-defined points of inflection: at pH 5, 8, and 12 after the neutralisation of 2·75, 4·5, and 7·6 acid dissociations, respectively. On

alkaline hydrolysis by standing at pH 12 for several days, 3·7 acid dissociations were titrated at pH 5, and 8·6 at pH 8 (curve XIII).

The deaminated yeast ribonucleic acid undergoes hydrolysis when its aqueous solution is heated. After 10 minutes' hydrolysis at 70° curve XI was obtained, and after 10 minutes or longer at 100° curve XII was obtained; no further liberation of acid groups occurred however long the time of hydrolysis. Curve XII indicates that one acid dissociation per tetranucleotide, titrated over the range pH 5—8, has been liberated by this hydrolysis.

*Discussion.*—The titration curve of yeast ribonucleic acid is not in agreement with the theoretical curve constructed from the known dissociation constants of the four primary phosphoric acid dissociations of the

FIG. 1.

*The titration curves of various samples of yeast ribonucleic acid.*

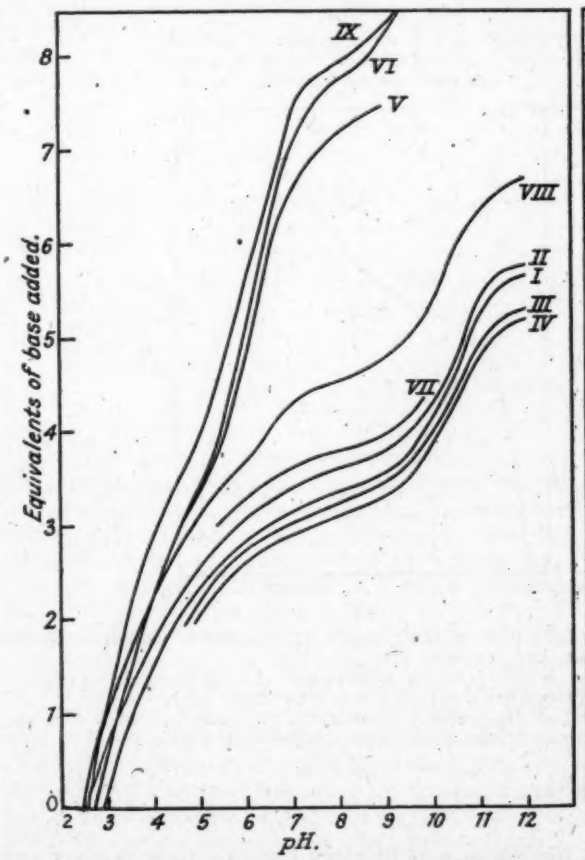



FIG. 2.

*The titration curves of deaminated yeast ribonucleic acid.*

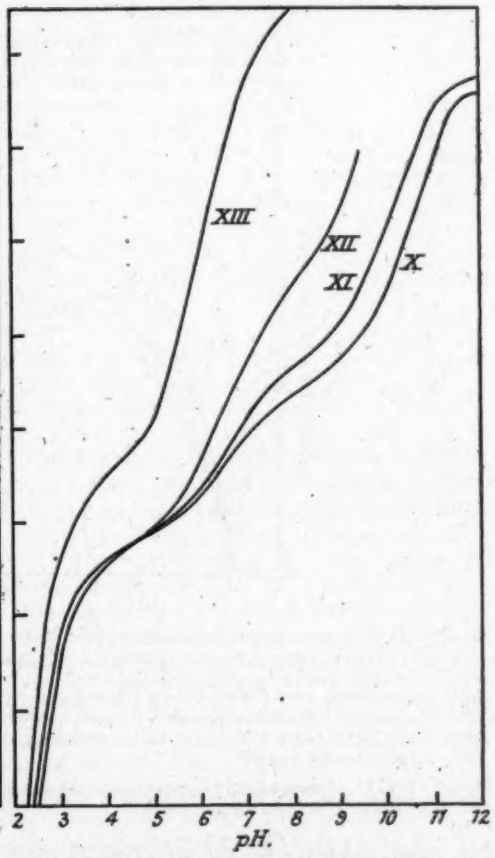



FIG. 1.—I, B.D.H.; II and VII, Boehringer; III, Merck; IV, Eastman. Back titration of the products of alkaline hydrolysis, V, B.D.H.; VI and IX, Boehringer; VIII, product isolated after the milk alkaline hydrolysis of Boehringer acid.

FIG. 2.—X, Deaminated yeast ribonucleic acid; XI, after hydrolysis at 70° for 10 minutes; XII, after hydrolysis at 100° for 10 minutes; XIII, back titration of the products of alkaline hydrolysis.

nucleotides guanylic, adenylic, uridylic, and cytidylic acid [p$K$: 2·3, 3·7, 1·0, and 4·2, respectively, as found by Levene and Simms (*J. Biol. Chem.*, 1925, **65**, 519) and confirmed by us], as shown by comparing curves XIV and XVII in Fig. 3, where curve XIV has been constructed from 0·4 equiv. of uridylic acid and 1 equiv. each of the three nucleotides guanylic, adenylic, and cytidylic acids, and curve XVII is the experimental curve obtained for B.D.H. yeast ribonucleic acid. This disagreement is always found however the 3·4 equivs. are chosen from the four nucleotides. This leads to the conclusion that one at least of the acidic groups of yeast ribonucleic acid must be a secondary phosphoric acid dissociation, and when curves are constructed on this basis, much closer agreement with the experimental results is obtained. This conclusion necessarily infers that one of the four atoms of phosphorus present in the tetranucleotide possesses no free acidic group, all taking part in internucleotide bonds. Furthermore, one phosphorus atom will have two free acidic groups and will be singly linked as in a nucleotide. Curves XV and XVI were constructed on this basis. The secondary dissociation constant of the phosphoric acid group was taken as having p$K$ 6·0 for all the nucleo-

tides (Levene and Simms, *loc. cit.*; confirmed by us). For curve XV the presence of 0·7 equiv. of uridylic acid, 1·0 equiv. of guanylic and cytidylic acids, and 0·7 equiv. of a secondary group was assumed. It will be seen that a point of inflection occurs in curve XV at pH 4·5: this is always found in the theoretical curves when the primary group of uridylic acid is included. Curve XVI is a much more faithful reproduction of the experimental curve (XVII), and has been constructed on the assumption of the presence of 1 primary acidic dissociation of guanylic and adenylic acids and 0·7 equiv. each of the primary and the secondary dissociation of cytidylic acid; other distributions of the 2·7 equivs. among the nucleotides adenylic, guanylic, and cytidylic acids lead to curves closely similar to curve XVI. It would thus appear probable that the triply bound phosphorus atom is that of uridylic acid. Allen and Eiler (*loc. cit.*) realised that, in order to explain the titration curve obtained by them for yeast ribonucleic acid, one of the primary acid groups would have to have a lower dissociation constant than that normally accepted for the primary phosphoric acid group of a nucleotide, and they suggested that the ionisation of the fourth group was depressed by the ionisation of the other three phosphoric acid groups.

FIG. 3.

*Comparison of the experimental and theoretical titration curves of yeast ribonucleic acid.*

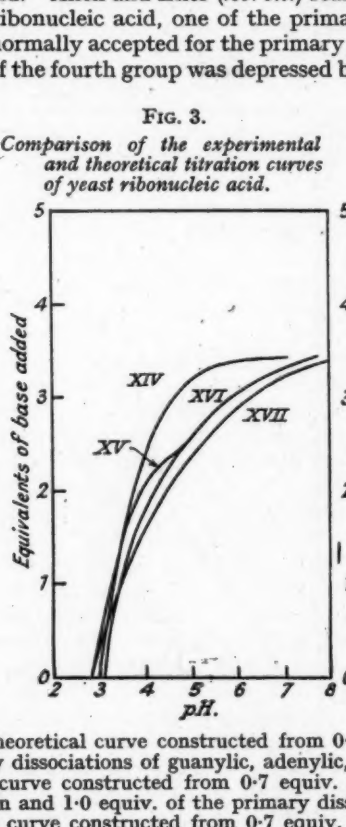



FIG. 4.

*Comparison of the experimental and the theoretical titration curve of deaminated yeast ribonucleic acid.*

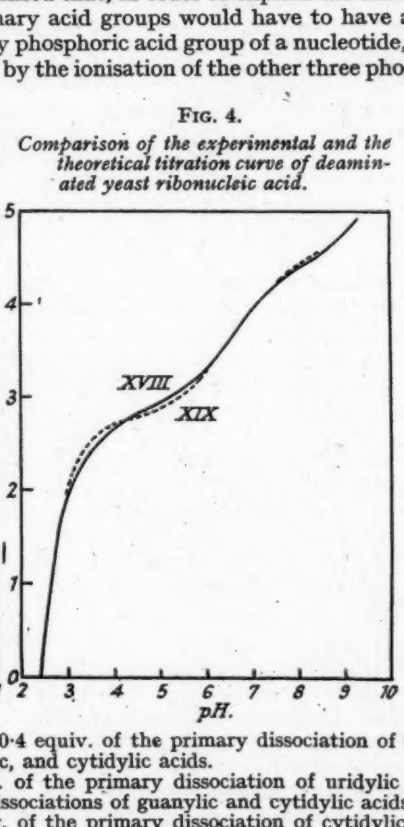



FIG. 3.—XIV. Theoretical curve constructed from 0·4 equiv. of the primary dissociation of uridylic acid, and 1·0 equiv. of the primary dissociations of guanylic, adenylic, and cytidylic acids.

XV. Theoretical curve constructed from 0·7 equiv. of the primary dissociation of uridylic acid, 0·7 equiv. of a secondary dissociation and 1·0 equiv. of the primary dissociations of guanylic and cytidylic acids.

XVI. Theoretical curve constructed from 0·7 equiv. of the primary dissociation of cytidylic acid, 0·7 equiv. of a secondary dissociation and 1·0 equiv. of the primary dissociations of guanylic and adenylic acids.

XVII. Experimental curve.

FIG. 4.—XVIII. Experimental curve (continuous line).

XIX. Theoretical curve (broken line).

Very strong evidence for the structure of yeast ribonucleic acid in which there are three primary and one secondary acid dissociations per tetranucleotide is given by the titration curve of the deaminated yeast nucleic acid. The removal of the amino-groups increases the dissociation of the primary acidic groups, and further, the hydroxyl group of xanthylic acid in the 2-position of the purine ring is titrated in the pH range 6—8. Ogston (J., 1935, 1376) gives for the dissociation constant of the purine hydroxyl group of xanthosine, the value of p$K$ 7·0, which has been confirmed by us. These two facts lead to the formation of a marked point of inflection at pH 5 after the titration of 2·75 primary phosphoric acid dissociations (Fig. 2, curve X). At pH 8 there is a second point of inflection after the titration of 0·75 secondary dissociation and the purine hydroxyl of xanthylic acid. The titration of the hydrolysis products of the deaminated acid (curve XIII) confirms the presence of 3·8 primary phosphoric acid dissociations per tetranucleotide before hydrolysis. Furthermore, the titration curve may be very accurately reproduced theoretically, as shown in Fig. 4, on the assumption of the presence of three primary and one secondary phosphoric acid groups and one xanthine hydroxyl group. The dissociation constants of the deaminated purine nucleotides have not so far been determined. These acids are unstable in aqueous solution, undergoing hydrolysis to xanthine or hypoxanthine and a ribose phosphoric acid (Levene and Dmochowski, *J. Biol. Chem.*, 1931, **93**, 563; Levene and Harris, *ibid.*, 1932, **95**, 755; 1933, **101**, 419). The graph has therefore been constructed by assuming a dissociation constant of p$K$ 1·0 for the primary acid dissociations, this being the value for uridylic acid. Slight changes in value of the dissociation constant in this range make insignificant differences in the position of the calculated curve.

There is a general tendency throughout the literature for the values of the phosphorus analyses of nucleic acids to be low, and this is accompanied by low titration data. An explanation of these facts now becomes possible, and is confirmed by the results obtained by introducing a correction for the missing phosphorus. The above titration data indicate the presence of a singly linked phosphorus atom, which thus possesses two free acidic groups. This atom could be removed without affecting the structure of the polynucleotide. This state of affairs could exist in the native acid, or removal could occur during some stage in the extraction and the subsequent purification process by either an enzymic or a hydrolytic fission. From the comparison of the experimental and theoretical curves, it is quite clearly shown that it is the secondary phosphoric acid group which has a low equivalent value. The theoretical phosphorus analysis per tetranucleotide is 9·5%, or per phosphorus atom 2·38%. The percentage of phosphorus linked by a single bond is therefore (for sample Y1) $8{\cdot}8 - 3 \times 2{\cdot}38 = 1{\cdot}66\%$. Thus the total number of acid groups present per tetranucleotide will be $2 + 1{\cdot}4 \times 2{\cdot}38/1{\cdot}66 = 4{\cdot}01$, in agreement with the theoretical number. By means of this method of correction, the number of acid groups per tetranucleotide has been calculated for the various samples examined. These values are given in the table, together with the uncorrected values for comparison. It will be noticed that the corrected values are very nearly whole numbers, except in the case of Merck and Eastman samples of yeast ribonucleic acid, which give anomalous results.

| | | Groups titrated to | | | |
|---|---|---|---|---|---|
| | | pH 5. | | pH 8. | |
| Sample of yeast ribonucleic acid. | P, %. | uncorr. | corr. | uncorr. | corr. |
| B.D.H. Y1 | 8·8 | — | — | 3·4 | 4·01 |
| ,, Y2 | 8·6 | — | — | 3·4 | 4·28 |
| ,, Y21 | 8·8 | — | — | 3·4 | 4·01 |
| ,, Y8 | 8·9 | — | — | 3·4 | 3·90 |
| Boehringer BY1 | 9·1 | — | — | 3·6 | 3·95 |
| Eastman Y9 | 8·9 | — | — | 3·2 | 3·62 |
| Merck Y10 | 9·3 | — | — | 3·3 | 3·43 |
| Deaminated B.D.H. DY33 | 8·9 | 2·75 | 3·01 | 4·5 | 5·03 |
| ,, DY1 | 9·0 | 2·75 | 2·96 | 4·5 | 4·92 |
| ,, DY5 | 8·9 | 2·75 | 3·01 | 4·5 | 5·03 |

It has been assumed in the above discussion that the four nucleotides, adenylic, guanylic, cytidylic, and uridylic acids, are present in yeast ribonucleic acid in equal proportion. The titration data give some evidence in support of this view. It is shown that yeast ribonucleic acid contains two acid dissociations which are titrated over the pH range 10—12; these are considered to be the nuclear hydroxyl groups of guanylic and uridylic acids, or the two groups present in two molecules of one of these acids. The titration of the deaminated acid indicates that an additional group per tetranucleotide is titrated over the pH range 5—8, which is considered to be the xanthosine hydroxyl group. These data indicate that there is one molecule of guanylic acid and one of uridylic acid present per tetranucleotide. No information can be obtained concerning the relative proportions of adenylic acid and cytidylic acid unless the ratio of purine to pyrimidine is taken to be unity. The results of Jones (" Nucleic Acids," 1920, p. 40, Longmans Green and Co., London), Hoffman (*J. Biol Chem.*, 1927, **73**, 15), Steudel (*Z. physiol. Chem.*, 1936, **242**, 100), Kobayashi (*J. Biochem. Japan*, 1932, **15**, 261), and of Ellinghaus (*Z. physiol. Chem.*, 1927, **164**, 261) tend to indicate that this ratio is unity. If this be so, then it follows that there are equal proportions of the four nucleotides present in the polytetranucleotide.

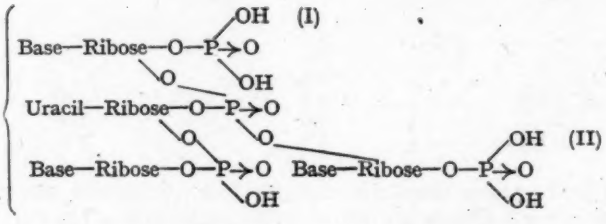
In Part VII it has been shown that the molecular weights of ribonucleic acid and of deaminated ribonucleic acid are approximately equal, and correspond to polynucleotides built up from 8—18 tetranucleotides. This is in agreement with the suggestion of a tetrabasic tetranucleotide, containing one triply linked phosphorus atom; of the four acid groups taking part in the formation of linkages, three will form inter-nucleotide links and the fourth an inter-tetranucleotide link. Further information concerning the groups taking part in the internucleotide links is forthcoming from a study of the products of mild hydrolysis. By carrying out the process of mild alkaline hydrolysis of yeast ribonucleic acid as described by Bredereck and Hoepfner (*loc. cit.*), a product having an approximate molecular weight of 5810 was isolated. The titration curve of this substance is given in Fig. 1, curve VIII, which indicates that the hydrolysis has broken linkages incorporating secondary phosphoric acid groups, since there is an increase in the number of groups titrated over the pH range 5—8. This suggests that if it were possible to isolate a tetranucleotide as claimed by Bredereck and Hoepfner, the pentabasic acid obtained would consist of three primary acid dissociations and two secondary acid dissociations. This view is substantiated by the mild hydrolysis of the deaminated acid, which on being heated to 100° liberates a secondary phosphoric acid dissociation as shown in curve XII, Fig. 2, the molecular weight of the hydrolysis product being of the order of 1800, although the isolation of the deaminated tetranucleotide free from purine has so far proved impracticable.

Bredereck and Hoepfner (*loc. cit.*) have prepared a deaminated tetranucleotide which, on titration to the phenolphthalein end-point, they found to be only pentabasic, and on back-titrating the products of alkaline hydrolysis (as distinct from the mild alkaline hydrolysis, described above), they have found only 8 acid groups. As is shown above, the xanthine hydroxyl group of deaminated guanylic acid is titrated over the pH range 5—8, and the acid, if it were a deaminated tetranucleotide should have been hexabasic. We have confirmed that

this hydroxyl group is titrated when titrating to the phenolphthalein end-point by titrating our sample of deaminated acid and finding 4·5 equivs., in agreement with the electrometric data. The results of Bredereck and Hoepfner can be explained by assuming that their supposed tetranucleotide was in fact a polytetranucleotide or that deamination was not complete, although their analysis does not suggest the latter explanation.

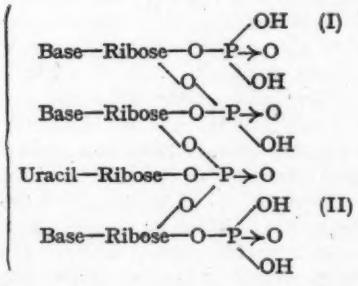
The experimental data given above suggest that yeast ribonucleic acid is a polynucleotide probably built up of tetranucleotide units, although the existence of the tetranucleotide as a chemical entity cannot be considered as proved until such a substance has been satisfactorily isolated. Each tetranucleotide present in the polytetranucleotide possesses three primary and one secondary acid dissociations, a second secondary acid dissociation being liberated on mild hydrolysis accompanied by a decrease in the molecular weight. These observations are not in agreement with the previously suggested formulæ for yeast ribonucleic acid. Feulgen's formula (*Z. physiol. Chem.*, 1918, **101**, 288) requires four primary dissociations per tetranucleotide, that of Levene and Simms (*J. Biol. Chem.*, 1926, **70**, 327) four primary and one secondary dissociation per tetranucleotide, and the cyclic formula of Takahashi (*J. Biochem. Japan*, 1932, **16**, 463) requires four primary dissociations per tetranucleotide. These formulæ have been fully described and discussed by Gulland (J., 1938, 1722). Polymerisation on the basis of Feulgen's or Takahashi's formula would produce polytetranucleotides having a maximum of three primary dissociations per tetranucleotide. On the other hand, the polymerisation of Levene and Simms' tetranucleotide would yield a polymer possessing either four primary dissociations, if linkage occurred through the secondary acidic group, or three primary and one secondary dissociation, if linkage occurred through a primary group. Although the latter result is in agreement with our titration data of yeast ribonucleic acid and deaminated yeast ribonucleic acid, it is not in agreement with our observations of the nature of the group liberated on mild hydrolysis. Possible formulæ which are in agreement with the observed data are given in (A), (B), and (C) below. Polymerisation would occur either through the group (I) or the group (II) to form the polytetranucleotide.

(A.)

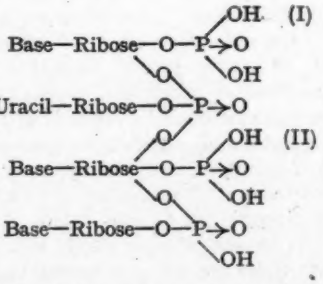



or

(B).




(C.)




It is important that such a formula should be compared with the existing enzyme data. Allen and Eiler (*loc. cit.*) observed that by the action of ribonuclease a secondary phosphoric acid group was liberated from yeast ribonucleic acid. They were uncertain whether the link was involved in ring formation, as in the formula of Takahashi, or in an inter-tetranucleotide link as in a polymer. It appears probable that the link broken by the enzyme ribonuclease may be the link broken on mild hydrolysis of ribonucleic or deaminated ribonucleic acid, which would then indicate that ribonuclease was a depolymerase. This could be proved by isolating the product after the action of ribonuclease and determining the molecular weight. Gulland and Jackson (J., 1938, 1492) found that the action of purified enzyme preparations containing a phosphomonoesterase and a diesterase produced 75% dephosphorylation of yeast ribonucleic acid, and further (unpublished result) that the mixed mono- and di-esterase produced only 75% dephosphorylation after the treatment of the yeast ribonucleic acid with an extract of boiled pancreatin which acts as a depolymerase. This indicates that one phosphorus atom is neither a di- nor a mono-ester, in agreement with the suggestion given above for the presence of one triply linked phosphorus atom per tetranucleotide. The action of bone phosphomonoesterase alone only liberated a maximum of 7% of the total phosphorus, from which Gulland and Jackson (*loc. cit.*) inferred the absence of a phosphomonoester group. This is not in agreement with the possible formulæ, and an explanation may lie in steric inaccessibility or enzyme specificity.

It is proposed to extend this investigation to other nucleic acids.

## Experimental.

The titration vessel consisted of a 100-c.c. Hysil bolt-head flask fitted with a rubber stopper suitably bored to accommodate two hydrogen electrodes, or a glass electrode, two hydrogen inlet tubes, an agar–saturated potassium chloride bridge,

and a stirrer. Of the two hydrogen inlet tubes, one passed hydrogen through the solution and the second maintained an atmosphere of hydrogen in the flask above the liquid, thus preventing contamination with atmospheric carbon dioxide. Mechanical stirring was generally found to be unnecessary, the steady stream of hydrogen efficiently stirring the solution. When the glass electrode was used, the hydrogen was replaced by carbon dioxide-free air.

The platinum wire electrodes were plated by a similar method to that described by Popoff, Kunz, and Snow (*J. Physical Chem.*, 1928, **32**, 1056). The electrodes were gold plated from a 1% gold chloride solution by means of a current of 8 milliamps., the gold surface was then polished with a smooth glass rod, and platinum black deposited from a 2% platinic chloride solution containing 0·02% of lead acetate by passing a current of 30—40 milliamps. for one minute. The electrodes were finally made the cathode in an electrolytic cell, containing dilute sulphuric acid, for 15 minutes, and then thoroughly washed with distilled water. Two such electrodes were used throughout all titrations, and if disagreement was greater than 1 mv. they were replaced. Freshly plated electrodes were used for each titration. The hydrogen, obtained from a cylinder, was purified by passage over red-hot copper (freshly reduced copper oxide), then over soda-lime, and it was finally washed, first with dilute sodium hydroxide solution and then with distilled water, both wash-bottles being contained in the thermostat.

The glass electrodes were of the bulb type described by Morton (*J. Sci. Instr.*, 1930, **7**, 187) and were calibrated in 0·05M-potassium hydrogen phthalate buffer (pH 3·97) before and after each titration.

The normal calomel half cell was connected with the titration vessel by an agar–saturated potassium chloride bridge. The calomel cell was periodically standardised with 0·1N-hydrochloric acid and 0·05M-potassium hydrogen phthalate. The value of the activity coefficient of the hydrogen ion in 0·1N-hydrochloric acid was taken as 0·841 (Scatchard, *J. Amer. Chem. Soc.*, 1925, **47**, 696). The e.m.f. of the calomel half cell so determined was 0·2820 ± 0·0005 v. The titration vessel and calomel half cell were immersed in an oil thermostat maintained at 25° ± 0·05°.

The measurement of e.m.f. was made by using a Cambridge valve potentiometer. A calibrated 5-c.c. Pyrex micro-burette, reading to 0·02 c.c., was used throughout.

The samples of yeast ribonucleic acid and deaminated yeast ribonucleic acid were prepared as described in Part VII (*loc. cit.*). These samples contained only negligible amounts of sodium and potassium as determined polarographically. Titrations of these acids were carried out by suspending in 50 c.c. of conductivity water approximately 0·25 g. of the solid, accurately weighed after being dried in a vacuum at 100° over phosphoric oxide to constant weight. Solution was brought about by the gradual addition of standard alkali with mechanical stirring. The addition of alkali was so controlled that the suspension did not become more alkaline than pH 6 at any time during the process of solution. From this point alkaline titrations to pH 12 or acid titrations to pH 2 were made with approximately 0·5N-alkali or -hydrochloric acid solution respectively. Sodium hydroxide was used when titrating using hydrogen electrodes, but potassium hydroxide was used when employing glass electrodes, as the alkaline errors of the glass electrode are very much lower in the presence of potassium ions (Jordan, *Trans. Faraday Soc.*, 1938, **34**, 1305). The hydrochloric acid was standardised gravimetrically by precipitation as silver chloride, and the alkali standardised by titration with the standard acid to the phenolphthalein and the methyl-orange end-point, and electrometrically. The two methods gave identical results.

The titration curves have been corrected in the strongly alkaline pH range for the amount of alkali required to produce the same pH in conductivity water alone (see Harris, *Proc. Roy. Soc.*, 1924, **95**, *B*, 440; Kirk and Schmidt, *J. Biol Chem.*, 1929, **81**, 237).

The addition of alkali or acid during a titration was so controlled that the determination of the pH of the solution was made at intervals of approximately 0·2 pH unit.

*Analyses.*—All samples were dried at 110° in a vacuum over phosphoric oxide.

Found in :

| | Y1. | Y2. | Y21. | Y8. | Y9. | Y10. | BY1. | BY2. | BY21. | DY1. | DY33. | DY5. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| N, % ..... | 16·2 | 16·0 | 16·0 | 16·3 | 15·7 | 16·1 | 15·8 | 15·7 | 15·6 | 13·6 | 13·3 | 13·1 |
| P, % ..... | 8·8 | 8·6 | 8·8 | 8·9 | 8·9 | 9·3 | 9·1 | 9·1 | 8·8 | 9·0 | 8·9 | 8·9 |

Calc. for a tetranucleotide containing 1 mol. each of the nucleotides, adenylic, guanylic, uridylic, and cytidylic acids, *i.e.*, $C_{38}H_{47}O_{28}N_{15}P_4$: N, 16·3; P, 9·5. Calc. for a deaminated tetranucleotide containing 1 mol. of the nucleotides inosinic and xanthylic acids, and 2 mols. of the nucleotide uridylic acid, *i.e.*, $C_{38}H_{44}O_{31}N_{12}P_4$: N, 12·9; P, 9·5%.

We acknowledge with gratitude the help given by Miss K. W. Sullivan and Mr. H. E. Dibben in making preliminary investigations, by Mr. J. E. Still in carrying out the microanalyses, and by Mr. N. A. Hurt, of Genatosan Ltd., in analysing the samples of nucleic acids for sodium and potassium. It is a pleasure to record the help given by Imperial Chemical Industries Ltd., in the form of grants for chemicals and apparatus.

UNIVERSITY COLLEGE, NOTTINGHAM. [*Received, November 19th*, 1943.]

# OBITUARY NOTICES.

## PETER PHILLIPS BEDSON.

### 1853—1943.

PETER PHILLIPS BEDSON was born in Manchester on April 2nd, 1853, and died at Hove on April 2nd, 1943, at the age of 90 years. Of this long life 43 years were spent in teaching and for 22 years he lived in retirement. Entering Owens College, Manchester, he came under the influence of Roscoe, and it may be presumed that this, along with his native ability, stimulated by the award of the Dalton scholarship in 1875, decided him to embrace chemistry as a profession. Contributory to this decision was undoubtedly the connexion of his family with the wrought iron industry; for his father was the inventor of the continuous rolling mill, and it was his brother who, in 1905, took a leading part in the memorial ceremony to Cort, the inventor of the Puddling process, at Hampstead Church.

Bedson's early work was in the Roscoe tradition, his first publication dealing with the addition compounds of titanium tetrachloride and vanadium oxychloride with ethyl ether. Two years were spent at Bonn under Kekulé, and there Bedson investigated the products of the bromination and nitration of phenylacetic acid, as part of the scheme then being undertaken with a view to the synthesis of indigo. Returning to Manchester in 1878, he joined the chemical staff, where he worked for four years, and at the end of this time was appointed Professor of Chemistry at the Durham College of Science (later Armstrong College, now King's College), Newcastle-on-Tyne. Laboratories and equipment were there of a rudimentary kind, but this did not deter him from straightway undertaking experimental work. This, perforce, had soon to be abandoned temporarily on removal to new and more commodious quarters, which still constitute the main abode of the chemical department. In this busy period Bedson found time to translate, in collaboration with W. Carleton Williams, Lothar Meyer's " Modern Theories of Chemistry."

The major chemical industries of Tyneside and district at this time were those of sulphuric acid and alkali, lead, copper, iron, and the destructive distillation of coal; and there is little doubt that Bedson felt it a matter of duty to abandon the field of pure chemistry and to devote his talents, and such time as he could spare from teaching, to the study of subjects related to the local industries. It seems unquestionable that his choice was partly, at least, determined by humanitarian considerations. The scourge of the lead industry then was the poisoning of the workfolk, especially those engaged in the making of white lead, and Bedson collaborated with the late Sir Thomas Oliver in the study of this subject, his share of the work being, to a large extent, the extremely unpleasant task of determining the metal in the organs of the unfortunate victims. To this period belongs also the writing of the article on lead in Thorpe's " Dictionary of Applied Chemistry."

It is for his work on coal that Bedson is best known; and here he was concerned not with the carbonisation industry, nor at first with the chemistry of coal as a problem of purely chemical interest, but rather with extending our knowledge of the raw material in a manner which might benefit, in life and limb, those engaged in winning it. The dangerous nature of coal-dust, arising from its inflammability, was then forcing its attention on those concerned in coal-getting, and Bedson's early work was directed to the extraction and analysis of the gases occluded or enclosed in samples of the dust, which had been a source of trouble and danger in the coal-workings or at the screens. The presence of homologues of methane was indicated in some of the analyses—an important point, since their effect, if present in the firedamp, would be to lower its temperature of ignition, and, in addition, the lower explosive limit, in admixture with air, would contain less of the inflammable gas than would be the case if only methane were present. This work was extended in various ways, *e.g.*, to freshly-hewn coal, to the bright coal and dant separated from it, extraction at various temperatures under the mercurial pump, grinding of lump coal under these conditions, and absorption of air by the dust after the enclosed gases had escaped. Bedson was an ardent gas-analyst and he enjoyed the work of construction of his glass apparatus. Though not precisely an expert glass-blower (some of his apparatus being faintly reminiscent of Mr. Heath Robinson's creations), his plant usually stood up to the somewhat severe conditions of service required of it.

The study of the explosive inflammation of mixtures of coal-dust and air followed naturally upon that of the gases enclosed in coal, and the apparatus devised for the purpose (irreverently known in the department as the puff box) was demonstrated at meetings of the Institution of Mining Engineers. The retardation of inflammation by admixture of coal-dust with non-inflammable dusts was recorded in 1907. Though Galloway had made similar observations as early as 1887, and Garforth had been led to the same conclusions from his examination of the great explosion at the Altofts pit in 1886, it was not until 1908 that the Mining Association of Great Britain started the serious investigation of the subject, the work being continued at Eskmeals a few years later. The Home Office first issued regulations on stonedusting in 1920. The slow appreciation of the dangers of coal-dust in mines among those engaged in the industry is noteworthy, and Bedson's statement, at a meeting of the Institution of Mining Engineers in 1910, that " one of the objects of the experiments he had made was to familiarise people with the dangers of coal-dust " was thoroughly justified and gave a clue to the ideals underlying the work.

In the early nineties of last century Bedson's attention was turned to the chemical nature of coal—its proximate constituents—and he started a long course of study of the action of a great variety of reagents upon it, prominent among which were potassium permanganate and potassium chlorate, the latter in presence of hydrogen chloride. There was but little to show for all this work; for though numerous products were obtained,

some of promising appearance, their chemical individuality could not always be positively established. One thing was obvious from the chemical side, and that was the complexity of coal; and it is a curious circumstance that only a few hundred yards from the laboratory where these investigations were in progress, namely, in the Hancock Museum of the Natural History Society of Newcastle, the visual proof of this complexity existed in the form of some 90 micro-sections of coal, which challenge comparison with modern preparations, made by William Hutton in 1833, and only brought to the light of day a few years ago. Conviction of the great chemical complexity of coal led Bedson to study the action of organic solvents upon it, in the hope that thereby a preliminary separation of constituents might be effected, and this in turn led to the discovery of the considerable solvent action of pyridine on coal, which has proved of great value to later workers in this field.

The rapid expansion of the College in the early part of this century, along with the claims of administrative work, in which he became more and more immersed, and the paucity of post-graduate students, all conspired to limit Bedson's activity in research; and, indeed, it was practically brought to a close at the outbreak of war in 1914, for the College buildings were taken over as a hospital and the chemical department was scattered in several inadequate buildings, widely apart from one another. Return to the old haunts after the war brought no relief, for the energies of the staff were fully called upon to cope with the great inrush of students which then took place. Retirement to Purley, and later to Hove, brought a well-merited rest.

Bedson was in some ways fortunate in that his youth was passed in an age when one could aspire to become a chemist—without adjectival qualification. This he certainly did become, for he had a wide and full knowledge, along with a common-sense grip, of his subject, and his opinion on any relevant problem always commanded respect. As a teacher his main concern was with pure science, and he had little or no sympathy with technical education. The justification of this attitude is to be found in the success of so many of his students who took up positions in industrial chemistry after leaving college. Though somewhat deficient in the rhetorical arts, he was yet a good and clear lecturer, skilful at the blackboard, and an apt experimentalist, and he spent infinite pains in the preparation of lecture experiments. His teaching duties were ever his first consideration and hardly a day passed but that he visited every student in the laboratory, often spending a great deal of time in clearing up their difficulties. This undoubtedly gave him power over errant students and was partly responsible for the good order which was always maintained in the lecture-room. It was supplemented by a piercing eye which, directed towards an unruly or inattentive student, soon brought him to a semblance, at least, of receptivity. Viewing his activities as a whole, he did a great work for the College in the developmental stage from small beginnings to full university stature. The Redbrick Universities owe much to men of his stamp.

As a man Bedson was small and spare of body, but wiry and energetic, always cheerful, bating an occasional flare-up of temper, which however quickly subsided and left no malice or ill-feeling. He was always Peter, to students and staff alike, and the eternal boy in him was never much below the surface; as an old colleague put it, at one of the last staff dinners he attended, he was the Peter Pan of the College. J. A. SMYTHE.

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## HENRY GEORGE DENHAM.

**1880—1943.**

AMONG the outstanding men of science produced by New Zealand, the late Professor Henry George Denham occupied a special place. Rarely does it happen that the holder of a Chair of Chemistry and Rector of a University College, combines with these positions a life of such influence in the organisation of scientific research applied to national needs. Denham was an initial member of the New Zealand Council of Scientific and Industrial Research, succeeding Sir George Shirtcliffe in the Chairmanship of this body in 1934. In addition, he was Chairman of the Wheat Research Institute from its inception, and a member of the committees of the Dairy Research Institute and of the Wool Manufacturers' Research Association.

In University administration he played an equally important part. He was a member of the Senate of the University of New Zealand and of its Academic Board, composed of representatives of the four constituent University Colleges. For some years he was also Chairman of Governors of Canterbury Agricultural College. He assisted in the founding of the Australian Chemical Institute and of the New Zealand Institute of Chemistry, was a foundation Fellow of both and President of the latter in 1934 and 1935. In addition he was a Fellow of the Royal Society of New Zealand, a Fellow of the Australian and New Zealand Association for the Advancement of Science, and President of Section B of this Association in 1928. This may give an indication of the range of his interests and responsibilities.

Denham was a graduate of Canterbury University College, which he entered in 1901. Graduating first in Arts, he took the M.Sc. degree in 1906, carrying out research on the conditions for the combustion of methane on the surface of palladised asbestos and was awarded the 1851 Science Research Scholarship. This led him to Donnan at the new Muspratt Laboratories in the University of Liverpool, where he graduated D.Sc. During this period he was actively engaged in the pioneering application of the hydrogen electrode to the determination of the hydrolysis of salts, work which developed into an interest in the possibility of the existence of sub-salts of the transition elements and led, in later work at Liverpool, in New Zealand and at the University of Queensland, Brisbane, to the isolation of sub-salts of lead and bismuth. The sub-salts of lead were prepared by a general method involving the action of the vapour of the alkyl halide, acetate or sulphate, on lead suboxide, which was obtained by heating the oxalate under reduced pressure. Leaving Liverpool for a period, he proceeded to Bredig at Heidelberg, working on heterogeneous catalysis, in particular that of the interaction

of titanous and hydrogen ions, and of the reduction of hydrogen cyanide to methylamine, and in due course receiving the Ph.D. degree. His interests in inorganic chemistry during this period were also exemplified by papers on the anomalous transport numbers observed, due to formation of complex ions, in solutions of copper chloride, copper bromide and cobalt bromide. Of these days both at Liverpool and at Heidelberg he retained the liveliest and warmest memories.

After returning to New Zealand, he proceeded to the University of Queensland, Brisbane, as lecturer in Chemistry and when Professor Steele went to England in connection with war industry, Denham became Acting-Professor. In 1921, he was appointed Professor of Inorganic Chemistry at Capetown. It was at this time that his textbook " An Inorganic Chemistry " was published, a third edition of which appeared in 1939. After two years at Capetown, he accepted the invitation to return to Canterbury University College in succession to his former teacher, Professor W. P. Evans. The experience as Professor of Chemistry in three Dominions was undoubtedly most valuable in the field of University administration and twenty years of University work at Canterbury College culminated in his appointment as Rector in 1941.

In 1936, two years after he had been appointed Chairman of the Council of Scientific and Industrial Research, he spent a sabbatical year in Great Britain and the United States, accompanied by Mrs. Denham, renewing old friendships and seeing something of other national research institutions. It was on the occasion of his visit to Great Britain that I first met him, a man of tall, active figure and of thoughtful manner which could be readily tempered by a warm smile. Later I had the privilege of knowing him well. Always approachable, he had a generosity of mind and an infectious enthusiasm and courage. These qualities were given full scope in his various fields of work. With the coming of the war, his activities as Rector, as Chairman of the Council of Scientific and Industrial Research and as member of the New Zealand Defence Advisory Committee, increased. Many nights had to be spent on the ferry steamer travelling the 200 miles to and from Wellington. Yet, despite the range and complexity of his interest, and the weight of his responsibilities, he remained his normal self, a delightful and stimulating companion. Particularly gratifying to his friends was the fact that he was able to enjoy, if only for a month, the honour the Society of Chemical Industry conferred on him in January in electing him to Honorary Membership. In making this election, the Council of the Society referred to his career, which, in the words of the citation " illustrates also the remarkable degree of influence which a man of scientific attainment can exert on the general life of the community when he is sufficiently public spirited to sacrifice all hope of leisure."

Although, however, his was a life of little or no leisure, he preserved a genuine interest in the problems of students, new and old, and it was probably this quality of courteous consideration that made his students feel that he was the true father of his Department and that not only was kindly shrewd advice always ready for the asking but that his interest followed them in their careers in New Zealand and overseas.

Recollections of his clear-cut personality and the warmth of his humanity are treasured by a wide circle, which includes former students, colleagues and friends. Now as time elapses after his death on February 15th at the age of 62, one realises even more fully the extent of the loss his death has occasioned to New Zealand chemistry, and to the academic and public life of this country. He leaves a widow and one son, who is on active service in the Middle East.

F. G. SOPER.

I am much indebted to Mr. J. Packer and Dr. H. N. Parton of the Chemistry Department, Canterbury University College, for information supplied.

F. G. S.

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## ALEXANDER LAUDER.

### 1870—1943.

ALEXANDER LAUDER died at Greenock, his birthplace, on November 11th, 1943, at the age of 73. He studied first under Professor Dittmar, in what is now the Royal Glasgow Technical College, and then with Professor Crum Brown at Edinburgh before taking up his first appointment as Assistant to Professor (later Sir J. J.) Dobbie in the newly founded University College of North Wales at Bangor.

In addition to assisting in the Chemistry Department he took up the study of Agricultural Chemistry and carried out experimental work, more particularly in connection with the field experiments. In conjunction with Professor Dobbie, he made an elaborate investigation into the alkaloids of *Corydalis cava* and worked out the constitution of these alkaloids—the results being published in a series of papers in the *Journal*, 1892—1904. Along with Professor Dobbie, he took up the study of absorption spectra and investigated the connection between the chemical constitution and the absorption spectra of certain organic compounds. With Professor Dobbie, he was a pioneer in this work.

In 1904 he was appointed Head of the Chemistry Department of the newly founded Agricultural College, Edinburgh, and in 1907 also became responsible for the teaching of Agricultural and Forest Chemistry to the University Degree Classes. In addition to his teaching, he carried out many investigations in various branches, giving particular attention to the composition of milk as affected by the feeding of the animal, the composition of swede turnips and heather and differences of a chemical nature in potato varieties. Most of that work was published in the *Scottish Journal of Agriculture* and in *Agricultural Progress* or in special reports. He retired in 1936.

Lauder had also a long record in administration, for he acted at various times as Secretary and Treasurer

to the College and as Director of Studies for four or five years immediately after the last war. He served on the Councils of the Institute of Chemistry and the Society of Chemical Industry, and was Chairman of the East of Scotland Branches of the Chemical Society and the Institute of Chemistry. He was prominently identified with the work of the Royal Society of Edinburgh and served on the Council for ten years and was Assistant Secretary to the Ordinary Meetings for five years. He also took an active share in the work of the British Association, being for a time Secretary of the Agricultural Section, and President of the Section for the Leicester Meeting in 1933, the subject of his address being " Chemistry and Agriculture."

Lauder was much interested in music and in English literature. He was a member of the Reid Orchestral Committee for many years, an active member of the Bach Society, and various other musical bodies. He had accumulated a library of standard English works, the study of which gave him much pleasure.

By those who knew him, he will always be remembered for the services he gave so ungrudgingly, for his sound judgment, for his wit and generous nature.

ALEX. M. SMITH.

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## ERNEST WILSON McCLELLAND.

### 1896—1943.

ERNEST WILSON MCCLELLAND was born on November 17th, 1896, the son of a schoolmaster teaching mathematics and science at the Model School, Belfast. From boyhood he suffered from the asthma which overshadowed his mature years, and, because of this, was home educated, by tutors who not only gave their son the grounding essential for his future career, but also stimulated his interest in a great variety of other subjects. Entering the Queen's University in 1914, McClelland graduated with a First in Chemistry in 1917, and was awarded a post-graduate studentship as the best man of his year. He subsequently joined the Aeronautical Inspection Directorate, and only in 1919 took up his deferred research studentship, going to work with Professor Smiles at Armstrong College, Newcastle-upon-Tyne. He followed the latter to King's College, London, in 1920 and a year later was awarded the degree of Ph.D. (Dunelm). For the next three years, he was a Senior Assistant at the Queen's University, under Professor Stewart, proceeding to the degree of D.Sc. at the end of this period. In 1924 he joined the staff of King's College, London, where he remained until his untimely death, at Bristol, on February 4th, 1943. The strain following on a successful effort to finish a rather heavy piece of examining work to time proved too much for his heart, weakened as it was by a lifelong and courageous fight with asthma.

McClelland was by nature a man of equable temperament and balanced mind. Forced, by his precarious health, to husband his strength, he had an air of deliberation, even slowness, which gave no clue to the vigour and healthy independence of his judgments, combined as they were with an ability, whilst dissenting, to weigh and appreciate the views of others. He was a man of great honesty and charity of mind, of indomitable cheerfulness however adverse the conditions, and a very staunch friend. His interests far transcended Chemistry, and his colleagues in the King's College Senior Common Room will not readily forget the dry and tolerant humour which characterised his talk. He made a very happy marriage, and is survived by his widow and a son.

Professionally, McClelland applied himself with equal zest to all aspects of his work. He was a successful teacher, both in the lecture room and in the laboratory, and his obvious competence, his devotion and inherent kindliness earned him a quite unsought-for popularity, both with students and with colleagues. His research work, which testified amply to his manipulative skill, lay essentially in the field of heterocyclic sulphur compounds, particularly in the study of derivatives of thionaphthen, benzthiazole and the benzthiazines, and nineteen papers by himself and his pupils appeared in the Journal between the years 1923—1941, subsequent to two joint publications with Professor Smiles. Many of his results in this field, recently somewhat neglected, remain at present unpublished, in particular, a number of examples where ring systems open with great ease, with subsequent closure to form new systems.

By McClelland's death, chemical science has lost an individual worker, one who followed his own bent without any particular thought to fame or to advancement, and who knew that research brings its own rewards. King's College, London, has lost a teacher who could be relied on implicitly in everything he undertook to do. As for his friends, they cherish of him many happy, and sometimes whimsical, memories. One of them recalls the interest " Mac " took in crime and criminology, and his working out, from data tabled in the " Hangman's Handbook," the exact drop which would be suitable for a man of his own height and weight. Another recollects meeting him in a bar in Belfast on Armistice Day, 1918, when " we caused a lot of amusement by getting a quiet corner table and playing a game of chess whilst Bedlam roared around." A third writes of how, when in a nursing home, McClelland " used to come down night after night to have a talk and help me to pass the evenings which, without him, would have been dreary indeed." Those who knew him will recognise these incidents as typical, and one not more than another.

A. J. ALLMAND.

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## HENRY FORSTER MORLEY.

### 1855—1943.

BY the death of Dr. Henry Forster Morley in his 88th year the Chemical Society lost one of its oldest members. He was elected a Fellow of the Society on December 18th, 1879, and served two periods of office as an ordinary member of council, *viz.*, 1887—1890 and 1896—1900.

Morley was born on October 25th, 1855, and was the eldest son of the late Henry Morley, LL.D., J.P., one time Professor of English Literature at University College, London. He was educated at the University College School and subsequently at University College, where he came under the influence of Professor A. W. Williamson. Morley has admitted in print how profoundly any success attained in his subsequent scientific career was due to the ideas instilled into him by Professor Williamson, who had probably as clear an insight into the fundamental principles of chemistry as any scientist then living.

Morley took his B.Sc. degree (1875) in the old London University and two years later the M.A. in mathematics. During this period his work led to his first paper—on the action of a Groves gas battery (*Phil. Mag.*, 1878). After graduating, Morley spent two or more years working in various laboratories on the Continent—first at Bonn (1878) under Prof. Kekulé, then under Prof. Baeyer in München (1879), next in 1880 at the École de Médecine, Paris, followed by a short time in the laboratory of Berlin University. Morley often expressed to the writer how much he owed to Kekulé, in particular, and also to Baeyer for his knowledge of structural organic chemistry. During his sojourn abroad, besides attending lectures, Morley, like most senior foreign students, took part in the research work being carried out in the various laboratories. His first work in Bonn—an attempt to replace the chlorine in $Cl{\cdot}CO{\cdot}CO_2Et$ by SH by hydrogen sulphide—had negative results, and he evidently turned to another subject, for in *Ber.* of 1878 a paper appeared by Dr. L. Claisen and H. F. Morley—Ueber eine neue Bildungsweise der Phenylglyoxylsäure—in which, by the interaction of ethyl oxalyl chloride and mercury diphenyl, the preparation of phenylglyoxylic acid was described and some account of its properties and of its ester given.

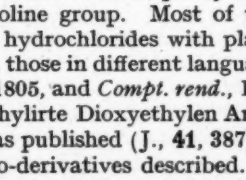
While in Munich Morley collaborated with Dr. C. Wurster—an Assistant to Baeyer—well known for his work on complex members of the amine group. In *Ber.*, 1879, **12**, 1514, Wurster and Morley described the preparation and properties of tetramethyl-*m*-phenylenediamine, which proved more stable than the corresponding *p*-derivative. It combined with methyl iodide, giving a crystalline compound,

$$N(CH_3)_2{\cdot}C_6H_4{\cdot}N(CH_3)_2,CH_3I$$

It readily reacted with bromine, forming a dibromo-derivative, isolated as crystalline dihydrochloride, $C_6H_2Br_2N_2(CH_3)_4,2HCl$. By the action of nitric acid they obtained a crystalline trinitro-compound containing one nitroso-group, $C_6H(NO_2)_3N_2(CH_3)_3{\cdot}NO$. This gave no Liebermann reaction and was stable to hot hydrochloric acid.

In the same year, Baeyer having suggested that a study of nitroso-derivatives of more complex amines might yield useful results, Morley undertook work in this field and chose as starting materials the easily available mono- and di-ethylenediphenyldiamines described by Hofmann. By the action of nitrous acid on ethylenediphenyldiamine Morley obtained a dinitroso-compound, $C_2H_4[N(C_6H_5){\cdot}NO]_2$. It formed no salts and gave no Liebermann reaction; and on reduction the original diamine was re-formed.

Diethylenediphenyldiamine was prepared by Hofmann's recipe but the yield was not so good as expected. On suitable treatment with nitrous acid a solid was formed difficult to purify; it proved to be dinitrosodiethylenediphenyldiamine. This gave no Liebermann reaction and was stable to alkalis. On reduction with tin and hydrochloric acid it gave in quantitative yield a beautifully crystalline base,



In 1880 Morley carried out a considerable amount of work, partly in Paris and partly in the laboratory of the Berlin University, on oxyamines of the choline group. Most of these amino-derivatives were isolated for analysis in the form of double salts of their hydrochlorides with platinum tetrachloride. An account of this work was published in the following journals, those in different languages covering more or less similar grounds: from the École de Médecine—*Ber.*, 1880, **13**, 1805, and *Compt. rend.*, 1880, **91**, 332, both on *iso*propyleneneurine; and from the Berlin laboratory—Ueber methylirte Dioxyethylen Amine, and covering much the same field in J., 1880, **37**, 232. In 1882 another paper was published (J., **41**, 387) on *iso*propyltoluidine: *n*- and *iso*-propyl compounds were compared and their nitroso-derivatives described.

On his return to London Morley was elected a Fellow of University College and Dean of a hostel for U.C. students founded by his father, who was Principal. During 1882 he devoted his time to the preparation of a thesis—A Study of the Amines—for London D.Sc., which he was awarded in the following year.

In 1883 Morley was appointed Assistant Professor of Chemistry at University College under Professor Williamson, a post which he held until Williamson was succeeded by Sir W. Ramsay in 1887. During this period Morley continued his researches with the help of senior students. In 1885 a paper appeared (J., **47**, 132) by H. F. Morley and A. G. Green on the constitution of common propylenechlorohydrin in which they showed it consisted mainly of $CH_3{\cdot}CH(OH){\cdot}CH_2Cl$, though simultaneous production of traces of its isomer was not excluded. In the same Journal (p. 134) they gave an account of experiments on the action of zinc ethide on the benzoate of propylenechlorohydrin. The reaction took an unexpected course and they discovered a new series of substances which they termed ketates. Instead of attacking the chlorine, the zinc ethide attached itself directly to the carbonyl group of the benzoyl radical, $C_6H_5{\cdot}CEt(OZnEt){\cdot}O{\cdot}C_3H_6Cl$. On elimination of the metal as chloroethide they obtained a substance which may be viewed as the propylene ether of phenyl ethyl orthoketone derived from orthoketone, $\begin{matrix}C_6H_5\\C_2H_5\end{matrix}\!\!>\!C\!<\!\!\begin{matrix}O\\O\end{matrix}\!\!>\!C_3H_6$ from $\begin{matrix}C_6H_5\\C_2H_5\end{matrix}\!\!>\!C(OH)_2$.

Later in the same year Morley and W. J. Saint published in the Journal an account of the preparation and properties of methyl ethyl thio-oxalate, $MeS{\cdot}CO{\cdot}CO_2Et$, by the action of methyl mercaptan on $Cl{\cdot}CO{\cdot}CO_2Et$. This work was in extension of Morley's unsuccessful experiments in his early Bonn days.

In 1887 he had some controversy with H. E. Armstrong (J., **51**, 579) on substitution in the benzene ring, but this is now of historical interest only.

Morley's last experimental work, as far as I have been able to ascertain, was undertaken in conjunction with E. Hori on *n*- and *iso*-propyl-*p*-toluidine (J., 1891, **59**, 33). In this paper they compare various salts and nitroso-derivatives.

After leaving University College, Morley in 1888 was appointed Professor of Chemistry at Queen's College, London, a part time post which he retained until 1901. In 1894 he was also appointed Lecturer in chemistry and physics at the Medical School of Charing Cross Hospital, where he continued until the teaching of these subjects was given up some ten years later. After leaving Univrsity College, Morley undertook very little research and devoted his energies largely to the literary side of his subject. His first book—" Outlines of Organic Chemistry "—was published in 1886 by Messrs. J. A. Churchill & Co. Morley held strong views as to how such a book should be written. He insisted that chemistry is an inductive science and protested against the dogmatic teaching of structural formulæ, apparently then in vogue. In his preface he discusses the various methods that might be adopted, and finally decided on a plan of describing simple compounds in the order in which they may be synthesised so that any compound should be a product of the one before and a producer of the one after. In this way the truth of its formula should be self-evident. Unfortunately owing to the requirements of various Examining Bodies and for other reasons, he was obliged to include a number of substances that could scarcely be dealt with in such way within the limits of a small volume. However he produced an admirable little book which served a crying need and had a deservedly long and successful run.

His next important work was the revision of the famous " Watts's Dictionary of Chemistry " published by Longmans Green & Co. Twenty-five years had passed since the work was first published, and seven years since the second part of the last supplement. Mr. Watts had undertaken the revision, but unfortunately died. The revised edition was edited by Dr. H. Forster Morley and (the late) Professor M. M. Pattison Muir, assisted by a staff of specialists. It was found necessary to rewrite the whole work and make it a true Dictionary of Pure Chemistry. Stern condensation was necessary, as the huge mass of material to be recorded had to be compressed into four volumes of about 800 pages.

Muir was responsible for Inorganic and General Chemistry and Morley for the Organic portion. The new edition differed from the old in that all references to processes of chemical technology were omitted, as these were being dealt with in a new dictionary edited by the late Professor T. E. Thorpe. General articles on allied subjects were also omitted, and even details of analytical processes. The new work was criticised as lacking the general interest of the old—but with the space available, it is difficult to see how this could have been otherwise. However the new dictionary supplied a great and growing need. Even to-day it has its use, since it affords an easy and accurate reference book for those who require historical information on any subject up to the date of publication.

Morley is perhaps best known for his important work on the International Catalogue of Scientific Literature. The Royal Society had prepared catalogues of scientific papers which were printed at first by H.M. Stationery Office. Subsequently financial aid for this purpose was supplied by the Treasury and by private donors. Towards the end of the last century it was felt that the work was too big for the resources available and it was decided to call for international co-operation. Accordingly the Royal Society took action and eventually conferences of delegates appointed by foreign Governments were held in London in 1896, 1898, and 1900. A scheme was agreed at the last conference under which control of the publication was to be vested in an international committee. The Royal Society undertook publication and advanced the necessary capital on loan. The catalogue was to be published yearly in 17 volumes dating from Jan., 1902, and Dr. H. Forster Morley was appointed Director of the Central Bureau. This was a great success and, in 1904, a convention of 14 States decided to continue the work; in the following year the Royal Society agreed to publish and finance it for another 5 years. In 1910 a convention of 18 States decided on further publication to 1915 and on a further extension 1916—1920. The Royal Society continued the printing arrangement until the 15th issue, dealing with 1915, but in 1916 the work was suspended owing to war-time difficulties. After the war, considerable further difficulties were encountered in the way of resumption of the Catalogue and in 1922 an executive committee decided not to continue the enterprise, the Treasurer of the Royal Society was appointed Receiver, and the accounts were finally closed. All this must have constituted an arduous task for Morley and given full scope for his business and organising abilities.

After ceasing to teach at the Medical school, Morley continued to take an interest in medical education and his membership of the Board of Preliminary Medical Studies was continued in the class of " Other Persons " and he gave much valuable help during a critical period. He served as secretary of the Board 1929—1930 and as chairman 1931—1932. For many years Morley did a good deal of examining work for various Universities and qualifying Bodies. His first important Examinership in chemistry was in the Final Honour School of Natural Science, Oxford University. At the London University he frequently examined in chemistry in the Preliminary and Intermediate Medical Examinations, in which he always viewed the claims of his subject in sane perspective in reference to the whole medical curriculum. For many years he acted as examiner in

chemistry for the Society of Apothecaries and did not retire until his 84th year, though pressed to continue for another year.

Morley was a member of the British Association, and on several occasions functioned as secretary to the chemical section. He and his accomplished wife were frequent in their attendance at social scientific gatherings in London, particularly at the Royal Institution, where they customarily were present at conversaziones and at the evening meetings.

Morley was a Liveryman of the City of London, and a member of the Society of Apothecaries, of which he was one of the most senior members of the Livery. He had a discriminating liking for the good things of this world and rarely missed dinners at the Apothecaries Company, which in pre-war days was fortunate in the possession of a good cook and a quite remarkable cellar.

Morley was a man of happy disposition and retained until late in life a very boyish outlook, which the writer found very fascinating. He was a genial and kindly host and loved to welcome his friends at his house in Hampstead or at Midhurst often to view paintings by his accomplished wife. He will be greatly missed by many old friends. Nevertheless in spite of his apparent simplicity of character he was very shrewd and a first-rate organiser and man of business. The writer has often thought that had Morley taken to commerce instead of science he would have made a fortune, and in the City might have attained high civic dignity.

The death of his beloved wife a couple of months before his own must have been a great shock. His troubles were further added to by a bomb through his house at Midhurst. Fortunately nobody was injured—Morley was in his dining-room at the time—but his library was much disturbed and a number of his papers were lost.

J. A. Gardner.

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## WILLIAM COLEBROOK REYNOLDS.

### 1870—1940.

William Colebrook Reynolds, who died in his 71st year on March 20th, 1940, was a most distinctive personality. Scientific enthusiasm dominated his life from early youth until death. His earliest contact with Chemistry was when as a boy he began experimenting in his father's pharmacy in Harrogate and attended classes in the Mechanics' Institute in Leeds. He gained a scholarship at Dalton Hall, Manchester, later a National Scholarship at the Royal College of Science, finally taking his D.Sc. at London University.

His scientific interests were widespread. His earliest published paper appeared in the *Transactions* in 1898; it relates to the properties of double salts of potassium and copper. Among the results of interest to be found in his subsequently published papers are the following:

In conjunction with F. L. Pyman the isolation of a new alkaloid, meteloidine, and the reduction products of papaverine.

With Francis H. Carr, showing the wide variation in the sparteine content of *Cytisus scoparius* during different months of the year; proof that the specific rotation of an alkaloidal basic ion cannot always be calculated from that of its salts; and the characterisation and constitution of norhyoscyamine, an alkaloid occurring in various plants of the *Solanaceæ*.

He published in collaboration with W. H. Taylor papers on the decomposition of nitric acid by light and the theory of sulphuric acid manufacture.

Reynolds worked on disinfectants and it was probably this interest which led to his describing emulsions which can be inverted without change of composition by warming—a number of the inverted emulsions being capable of complete reversion. Subsequent work on interfacial tension led to two papers published in *Transactions* in 1921 in which an improved method of measuring interfacial tension by the capillary method is described.

Other interests which claimed Reynolds's attention were the structure of the atom. A book on "Atomic Structure as modified by Oxidation and Reduction," published in 1928, expounds his original views on changes in atomic structure during oxidation and reduction processes. Also he published in letters to *Nature* and in a paper in the *Journal* of the Society of Chemical Industry in 1930 results of his observations on atmospheric phenomena based on work carried out at his home in Upminster and during holidays in Switzerland.

In social activities he displayed the same thoroughness and enthusiasm as in his scientific work, organising horticultural and athletic activities; even in his sixties he played cricket and took a full share in bowling and batting. His wife, son and two daughters survive him.

Francis H. Carr.

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## SIEGFRIED RUHEMANN.

### 1859—1943.

Siegfried Ruhemann was well known to British chemists prior to the Great War of 1914—1918; from then on, after leaving this country until his death this year, his British friends lost contact with him, and the contact was not renewed on his return to England in 1939. When I was asked to write this obituary notice I felt that it was a revival of the old days of my association with him as a student and collaborator from 1888 to 1900. The stimulus given by him in fundmental research has had a great influence on many students, including myself, who look back on the time spent under his guidance as being of the highest value in their life work.

His enthusiasm, dogged perserverance and skill in manipulation were infectious. He was the pioneer of Organic Chemistry in the University of Cambridge in the days when research in that subject was not warmly encouraged.

Dr. Martin Ruhemann has kindly supplied me with details of his father's early life and of his later days. He was born at Johannesburg in East Prussia in 1859, where his father was in the leather trade, and was apparently one of the notables in the little place. When he was seven years old his father died and his mother a few years later took him to Berlin with his two elder brothers and several older stepbrothers and sisters. There was very little money and his father had great difficulty in working his way through the University. He took his degree in 1882 and worked for a short time with Professor Wichelhaus. He was very dissatisfied with his position and soon transferred to Professor Hofmann, for whom he preserved throughout the whole of his life a sincere respect and admiration. Professor Hofmann was asked by Sir James Dewar to supply an organic chemist from among his pupils and selected Siegfried Ruhemann.

Ruhemann was appointed Assistant to the Jacksonian Professor (Sir James Dewar) and delivered the elementary and advanced lectures in Organic Chemistry and soon collected a number of workers in the Laboratory. I am indebted to Dr. J. T. Hewitt for his recollections. He says, " I do not think that I met Ruhemann until after taking Part I of the Nat. Sci. Tripos in 1889, and never attended the celebrated course of lectures in Elementary Organic Chemistry. I started in his laboratory and went to his advanced course of lectures, which I thoroughly enjoyed. His accent was somewhat foreign, but he spoke English fluently, even if some of the expressions he used were literal translations of German equivalents. He always seemed to be as pleased in giving the lectures as the audience was in hearing them. Within a short time of the end of the lecture he came round the laboratory asking each individual who had been present, whether there was any further point that needed explanation. As a teacher of practical Organic Chemistry Ruhemann was even more in his element than in the lecture room.

" He had rooms at the top of the new chemical building, so that there was no need to be away for a long time at meals, and as soon as one of these was finished he could turn again to his beloved work. Added to this attention to research pure and simple, he was not much engaged in examining work and seemed to have no desire to make an extra income by side-lines, commercial or otherwise. This was all to the good so far as his students were concerned."

Numerous stories might be told of Ruhemann's idiosyncrasies in the lecture room and in the laboratory, for these have remained in the memories of both his elementary and advanced students, even to the present day. His dramatic style at the blackboard in the development of the formation of an organic compound was most striking, and often met with loud applause. As to his advanced course, there was unanimous appreciation of its value. In order not to interfere with his research work, the advanced lectures were at 9 a.m. and the elementary from 1 to 2 p.m., and in spite of these inconvenient hours the attendance was always large.

After some years differences arose between the Jacksonian Professor and his Assistant and these resulted in the appointment of Ruhemann to a University Lectureship in Organic Chemistry. In 1891 he removed to the Caius College Laboratory, where accommodation was found for his research students, now increasing in number, and for his senior students. Here he worked until 1908, when the College Laboratory was closed and Ruhemann returned to the University Laboratory, where he continued his advanced lectures, but not the elementary course, and with a much reduced number of collaborators.

He took British nationality in 1906 and in 1914 was elected F.R.S. for his valuable contributions to Organic Chemistry. During the first Great War he resigned his lectureship, and in 1919 returned to Germany.

The record of Ruhemann's work in Cambridge is striking. From 1888 to 1915 he published 94 papers either alone or with collaborators, and of these he had 27; 68 papers appeared in the *Journal*. The subjects dealt with were varied and included tetrazines, pyrimidines, pyrazolones, studies in β-ketonic acids, diketohydrindene hydrate as a test for α-amino-acids and protein derivatives, studies in cyclic ketones, etc. It was pioneer work and essentially exploratory in character; no reaction is named after him and he put forward no hypothesis nor engaged in any great controversy, for the accuracy of his results was generally admitted. The value of his work is inestimable and progress ahead is assured by such careful survey of unexplored regions.

From 1919 to his death his British friends for the most part lost sight of him, but it is evident from information supplied by his son that the fundamental research " urge " still persisted. His son writes as follows :—

" On his return to Germany in 1919, my father worked for a time on his own in Fischer's laboratory until, in 1921, he was put in charge of a research laboratory in Charlottenburg. It was called ' Braunkohlen und Mineralölforschungsinstitut ' and was run jointly by the Technical College and the ' Braunkohleninstitut.' When my father took this over it was quite small. The staff consisted of one technician, two students and a boy. He worked there for 10 years and built it up very considerably. When he left in 1933, there were well over a dozen people working there. He found it difficult at first to do industrial research, but at times I think he enjoyed it and published a number of papers. Working with seven collaborators, he published seven papers, chiefly in *Brennstoff-Chemie*.

After his retirement he lived peacefully in Zehlendorf for some years on his savings and a pension, and for long could not make up his mind to leave Germany, although he hated the new régime, but he felt too old to move. Finally, in May, 1939, only a few months before the war started, my father and mother returned to England. They had retained their British nationality and we lived for some years together in Muswell Hill. My father was taken ill early in August and died very soon and without much suffering. He felt during his last

years in England a very strong and sincere attachment to this country, and wished earnestly for an opportunity to express this to some of his old friends. Unfortunately infirmity prevented him from taking up old associates."

The record of Ruhemann's work is one of which any investigator might be proud. Chemists of the former generation who were his students will acknowledge a deep debt of gratitude to him as a teacher and as a stimulator in research. R. S. MORRELL.

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## PERCY WILLIAMS.

### 1873—1942.

PERCY WILLIAMS died in February, 1942, at the age of 69. He was born in 1873 in Hackney, his father, Robey Williams, being described as a mercantile clerk. His parents were deeply religious, and sent their son to a Chapel School in Lower Clapton. From school he passed on to the Alexandra Palace, where his early scientific training was obtained, but he owed his main education to Sir William Ramsay, under whom he studied at University College for several years. In a testimonial written some years later Ramsay refers to Williams' " exceptionally brilliant career and his great experience of research methods in many different branches of Chemistry " obtained in London, France and Germany, for after completing his work at Gower Street, to which reference will be made later, Williams used the proceeds of a South Kensington Scholarship to cross over to Paris, and to enrol in the team of chemists then working under Henri Moissan, with whom he remained for two years, collaborating in a number of researches on the preparation of borides of calcium, strontium and barium, a carbide of tungsten and a double carbide of tungsten and iron. The results were later presented to the Academy by Moissan.

In 1898 Williams migrated to Berlin, where he completed his education in the laboratory of J. H. van 't Hoff before returning to England for the purpose of taking up an industrial career.

His first employment appears to have been with the British Uralite Company of Higham, Kent, where he was in charge of the laboratory under the general direction of the late Gordon Salamon. In 1900 he journeyed to Russia on behalf of his Company, which, at that time, drew its supplies of asbestos from the Ural Mountains. In 1906 Williams left England to become chemist to the Borneo Rubber & Trading Company at their factory at Sockadana, where he first supervised the installation of a double-effect evaporating plant, and was later in charge of the production of quinine. In 1911 the factory was closed owing to the failure of the bark supply and Williams returned to England. For a time he worked under Professor Bone with the Bone-Court Combustion Company, and in 1914 he became chemist to the Aluminium Plant and Vessel Company Limited at Wandsworth, where he worked for the remainder of his life.

Williams' most important scientific contribution was the part he played in the joint research of Rayleigh and Ramsay which led to the isolation of argon by absorption of the nitrogen of the air by magnesium. Unfortunately, Williams could never be induced in later years to discuss the matter, but the present Lord Rayleigh has kindly informed the writer that he recalls that Sir William Ramsay told his father that he would like to make special mention of Williams in the paper they were about to publish, as he had been of the greatest help; that he (Ramsay) had told Williams to try magnesium and that Williams had carried out that part of the work without further guidance. Williams was, in fact, specially acknowledged, but exactly what form his assistance took it is now impossible to ascertain.

In all his work Williams was distinguished by the directness of the methods he evolved and the simplicity of the apparatus which he used to solve the innumerable problems with which he was confronted. Perhaps his method for determining the proneness of certain alloys to the form of corrosion which U. R. Evans has described as " crevice attack " may serve as an example. Separate drops of the corrosive fluid were placed upon the sample of the metal under investigation, and on each drop was placed a piece of glass rod about 2 cm. in length. Through these, of which if desired a large number could be placed on a small piece of metal, the development of the attack could be watched as through a magnifying glass. The atmosphere could be controlled by placing the specimens under a bell jar, filled with the appropriate gas.

Gifted with extraordinary manual dexterity, Williams was able to make almost all the utensils he needed, whether they were constructed of glass or metals. His reading was wide and catholic and his memory unfailing, whilst his scientific honesty drew from Henri Moissan the tribute " Je me rapelle . . . la façon consciencieuse et intelligente avec laquelle vous avez travaillé auprés de moi et l'honnêteté que vous apportiez à vos analyses." His ingenuity in devising his experiments and his pertinacity in carrying them through almost invariably brought definite results, and the writer can only remember one case among the hundreds presented to Williams during the course of 28 years, and ranging over a very wide field, in which the problem remained unsolved.

To his colleagues of all ages and many branches of science and industry he was unfailingly helpful, and no trouble was too great to enable him to meet the many demands which their confidence in him led them to make upon his time.

With Williams has passed one of those all-round chemists who are become distressingly rare in these days of intense specialisation.

He was elected a Fellow of the Chemical Society in December, 1907. RICHARD SELIGMAN.

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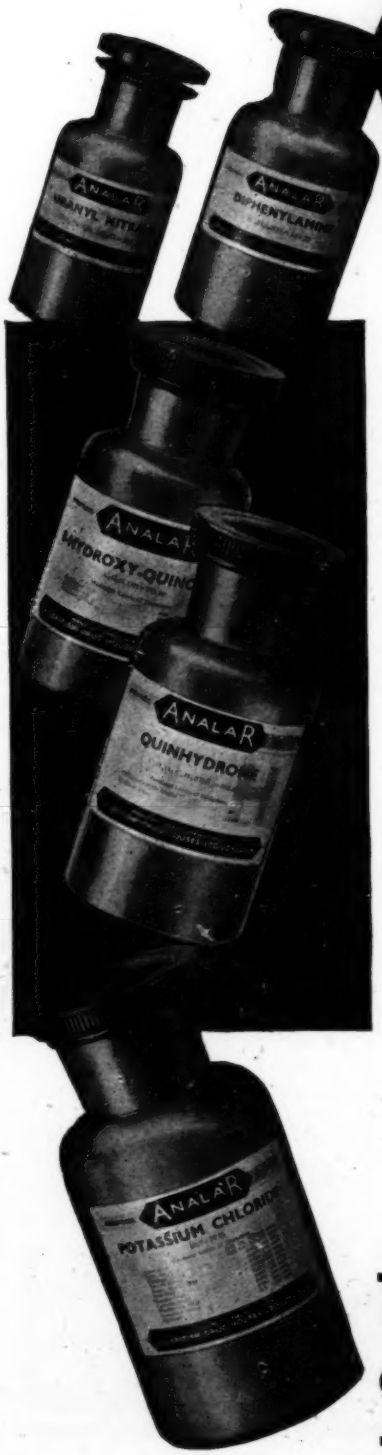


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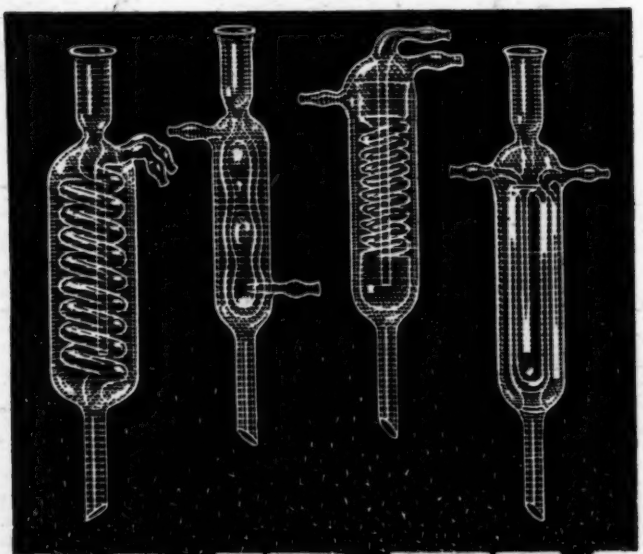

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